VOLUME 54 NUMBER 4 OCTOBER 1992 ISSN 0003-4975

H03462-26-P024824.

CM

26

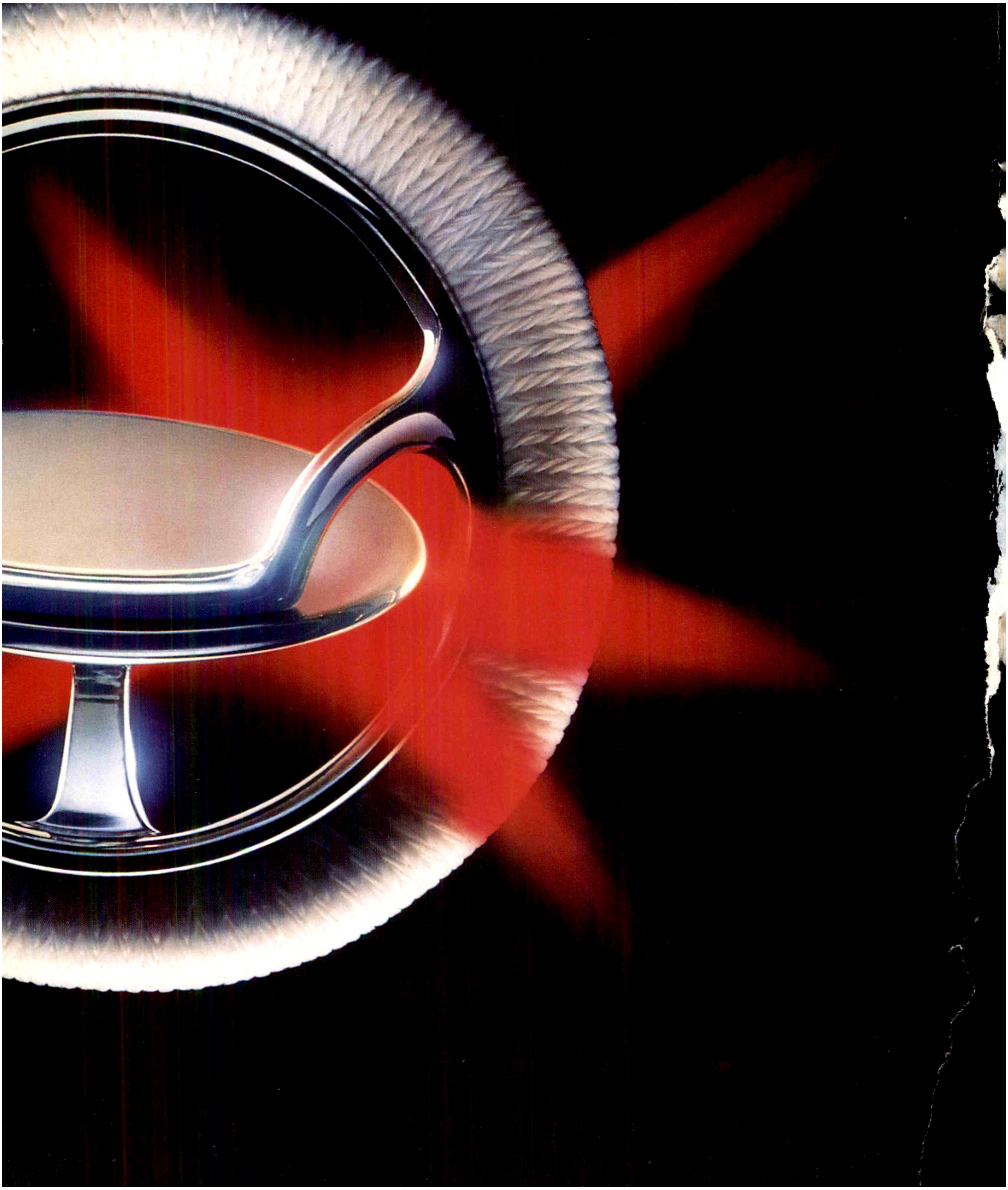
THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Thirty-ninth Annual Meeting of the Southern Thoracic Surgical Association
November 5–7, 1992, Saddlebrook Golf and Tennis Resort,
Wesley Chapel (near Tampa), Florida

Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons
January 25–27, 1993, San Antonio Convention Center, San Antonio, Texas

Elsevier



Volume 54 Number 4

THE ANNALS OF THORACIC SURGERY

October 1992

P, 24 824

Contents

Original Articles

Cerebral Blood Flow and Metabolism in Hypothermic Circulatory Arrest 609

Craig K. Mezrow, MS, Ali M. Sadeghi, MD, Alejandro Gandsas, MD, Howard H. Shiang, DVM, Dale Levy, MD, Robert Green, MD, Ian R. Holzman, MD, and Randall B. Griepp, MD

Does a Posterior Aneurysm Increase the Risk of Endocardial Resection? 617

Irving L. Kron, MD, John A. Kern, MD, Pierre Theodore, BA, Terry L. Flanagan, MPH, David E. Haines, MD, Michael J. Barber, MD, and John P. DiMarco, MD, PhD

Anomalous Left Coronary Artery From the Pulmonary Artery: Results of Isolated Aortic Reimplantation 621

Pascal R. Vouhé, MD, Daniel Tamisier, MD, Daniel Sidi, MD, Françoise Vernant, MD, Philippe Mauriat, MD, Philippe Pouard, MD, and Francine Leca, MD

Anterior Mediastinal Tracheostomy With and Without Cervical Exenteration 628

Mark B. Orringer, MD

Postpneumonectomy Syndrome: Diagnosis, Management, and Results 638

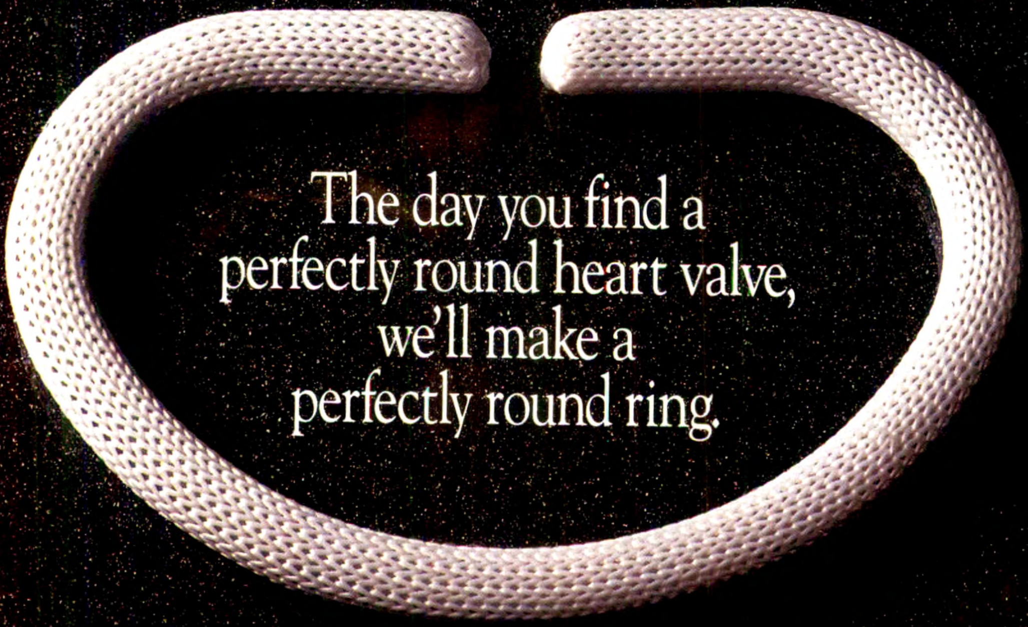
Hermes C. Grillo, MD, Jo-Anne O. Shepard, MD, Douglas J. Mathisen, MD, and David J. Kanarek, MD

Revival of the Radial Artery for Coronary Artery Bypass Grafting 652

Christophe Acar, MD, Victor A. Jebara, MD, Michele Portoghese, MD, Bernard Beyssen, MD, Jean Yves Pagny, MD, Philippe Grare, MD, Juan C. Chachques, MD, Jean-Noël Fabiani, MD, Alain Deloche, MD, Jean Leon Guermonprez, MD, and Alain F. Carpentier, MD, PhD

continued on page A-7

The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery*, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.



Carpentier-Edwards® Annuloplasty Rings.
The only rings designed for remodeling annuloplasty.

Edwards CVS Division

© Copyright 1990. Baxter Healthcare Corporation. All rights reserved.

Baxter

Continued from page A-5

Clinical and Hemodynamic Assessment of the Hancock II Bioprosthesis 661

Tirone E. David, MD, Susan Armstrong, MSc, and Zhao Sun, MA

Use of Epicardial Electrocardiograms for Detecting Cardiac Allograft Rejection 669

Eric D. Irwin, MD, Richard W. Bianco, BS, Rose Clack, BS, John Grehan, BA, David P. Slovut, MD, Raouf Nakhleh, MD, R. Morton Bolman III, MD, and Sara J. Shumway, MD

Predictive Criteria for the Need of Extracorporeal Circulation in Single-Lung Transplantation 676

Stephan W. Hirt, MD, Axel Haverich, MD, Thorsten Wahlers, MD, Hans-Joachim Schäfers, MD, Aiman Alken, MD, and Hans-Georg Borst, MD

Stentless Porcine and Pericardial Valve in Aortic Position 681

Riccardo Casabona, MD, Ruggero De Paulis, MD, Giuseppe F. Zattera, MD, Michele di Summa, MD, Walter Bottone, MD, Carla Stacchino, MD, Mario O. P. Vrandecic, MD, and Mario Morea, MD

Transhiatal Esophagectomy: A Safe Alternative for Selected Patients 686

Thomas M. Daniel, MD, Kirk J. Fleischer, MD, Terry L. Flanagan, MPH, Curtis G. Tribble, MD, and Irving L. Kron, MD

The Learning Curve for Intraoperative Echocardiography During Congenital Heart Surgery 691

Ross M. Ungerleider, MD, William J. Greeley, MD, Ronald J. Kanter, MD, and Joseph A. Kisslo, MD

Emergent Applications of Cardiopulmonary Support: A Multiinstitutional Experience 699

Jonathan G. Hill, MD, Pamela S. Bruhn, RN, BSN, Sheldon E. Cohen, MD, Michael W. Gallagher, MD, Frank Manart, MD, Charles A. Moore, MD, Paul E. Seifert, MD, Paul Askari, CCP, and Candace Banchieri, CCP

Effect of Light Dose on the Photodynamic Destruction of Endobronchial Tumors 705

James S. McCaughan, Jr, MD, Philip C. Hawley, MD, David G. Brown, MD, Gerard S. Kakos, MD, and Thomas E. Williams, Jr, MD

Nicardipine: Myocardial Protection in Isolated Working Hearts 712

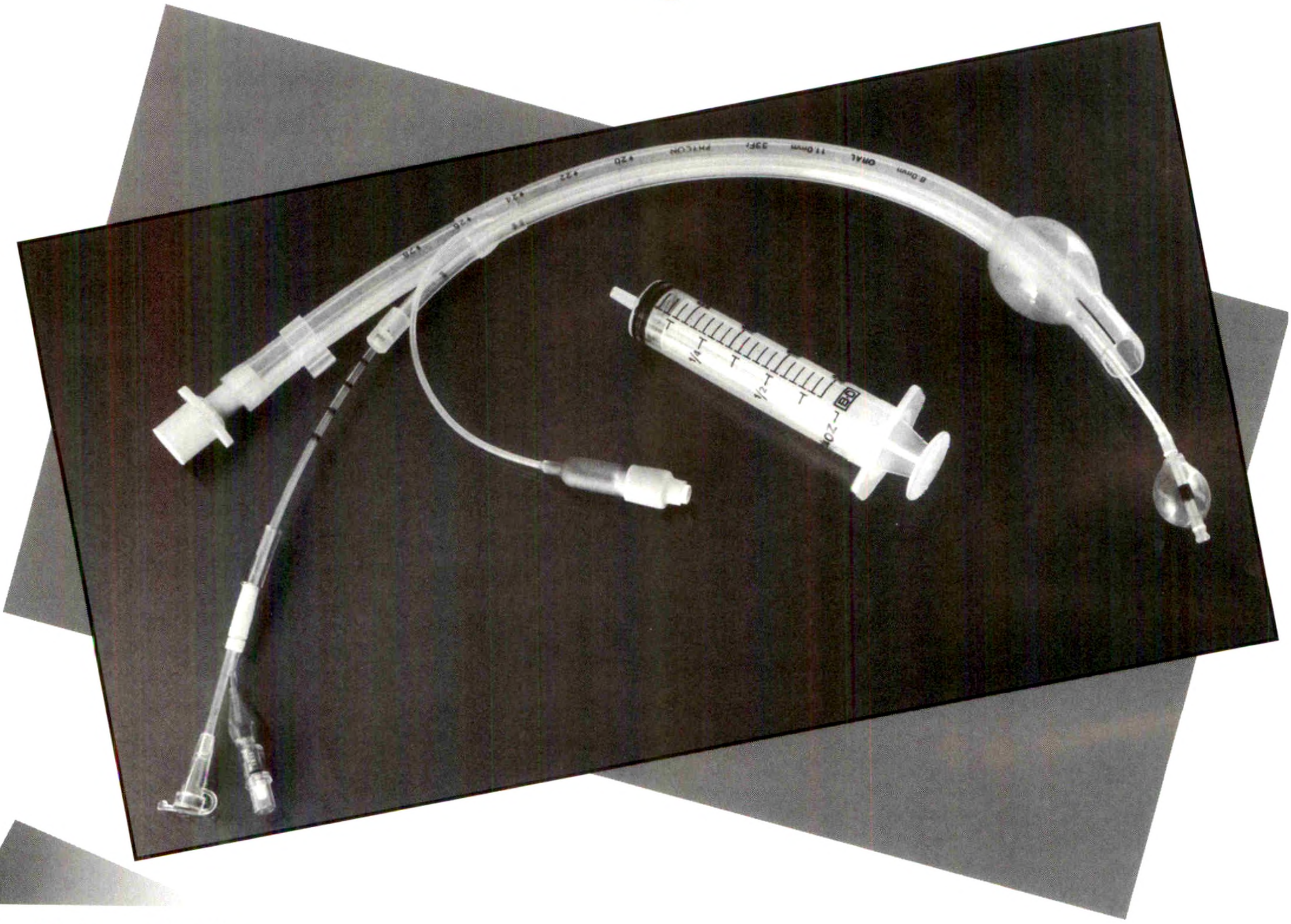
Marc E. Mitchell, MD, David A. DeBoer, MD, Michael D. Crittenden, MD, and Richard E. Clark, MD

Electrophysiologic Study of Dysrhythmias After Atrial Operations in Dogs 717

Tatsuo Tamiya, MD, Toshiyuki Yamashiro, MD, Atsushi Hata, MD, Kenshi Kuge, MD, Sohichi Asano, MD, and Takayuki Sato, MD

continued on page A-9

The New Concept For One Lung Anesthesia



The Univent® Tube

The Univent Tube facilitates surgery by collapsing the non dependent lung. It keeps free blood and secretions from flowing to the healthy lung.

The Univent Tube is a specialized endotracheal tube with an anterior channel housing a moveable blocker. The blocker has a lumen allowing insufflation, CPAP, suction, etc. The blocker is directed to either lung simply by rotating the tube assembly before inflation of the main tube cuff, then gently push the blocker into place under bronchoscopic guidance. The blocker can be secured to the tube assembly to restrict movement once positioned. By deflating the blocker and pulling it back into its' channel, Univent functions as a normal endotracheal tube for post-op ventilation.

Features

- Ideal for thoracoscopic procedures
- Facilitates diagnostic bronchoscopy to both lungs
- Quick and easy placement
- Made from medical grade silicone, will not irritate the mucosa
- No need to change tubes for post operative ventilation
- Blocker lumen supports suction, insufflation, CPAP
- Available in 7 sizes

VITAID
Leading Edge Medical Products
1-800-327-9301

For further information contact:

Vitaid
269 Portage Road, Lewiston, NY. 14092
In Canada Call (416) 488-4135

Continued from page A-7

Time for New Concepts About Measurement of Complement Activation by Cardiopulmonary Bypass? 725

Vibeke Videm, MD, PhD, Erik Fosse, MD, PhD, Tom Eirik Mollnes, MD, PhD,
Peter Garred, MD, PhD, and Jan L. Svennevig, MD, PhD

Congenital Malformations of the Coronary Arteries: The Texas Heart Institute Experience 732

Eugene D. Fernandes, MD, Hooshang Kadivar, MD, Grady L. Hallman, MD,
George J. Reul, MD, David A. Ott, MD, and Denton A. Cooley, MD

Exocrine Pancreatic Function in Mediastinal Teratomata: An Aid to Preoperative Diagnosis? 741

Panny Kallis, FRCS, Tom Treasure, FRCS, S. J. Keith Holmes, FRCS, and
Meryl Griffiths, MRCPath

Endotoxin Release and Tumor Necrosis Factor Formation During Cardiopulmonary Bypass 744

Nicolaas J. G. Jansen, MD, PhD, Willem van Oeveren, PhD, Y. J. Gu, MD,
Marilijn H. van Vliet, MD, Leon Eijsman, MD, PhD, and
Charles R. H. Wildevuur, MD, PhD

Temperature Monitoring During CPB in Infants: Does It Predict Efficient Brain Cooling? 749

Frank H. Kern, MD, Richard A. Jonas, MD, John E. Mayer, Jr, MD, Frank L. Hanley, MD,
Aldo R. Castaneda, MD, and Paul R. Hickey, MD

Surgical Management of Infective Endocarditis in Children 755

Michael Citak, MD, Allan Rees, MD, and Constantine Mavroudis, MD

Case Reports

Left Ventricular Diverticulum With Hypertrophy of the Left Ventricular Apex 761

Chojiro Yamashita, MD, Hiroomi Nakamura, MD, Satoshi Tobe, MD,
Toshihiro Koterazawa, MD, and Sinnichirou Yamamoto, MD

Chronic Fibrosing Mediastinitis and Superior Vena Caval Obstruction From Blastomycosis 764

Carl F. Lagerstrom, MD, Holly G. Mitchell, MD, Barney S. Graham, MD, PhD, and
John W. Hammon, Jr, MD

Saphenous Vein Graft Pseudoaneurysm Formation After Postoperative Mediastinitis 766

Julian A. Smith, FRACS, and Jacob Goldstein, FRACS

continued on page A-12

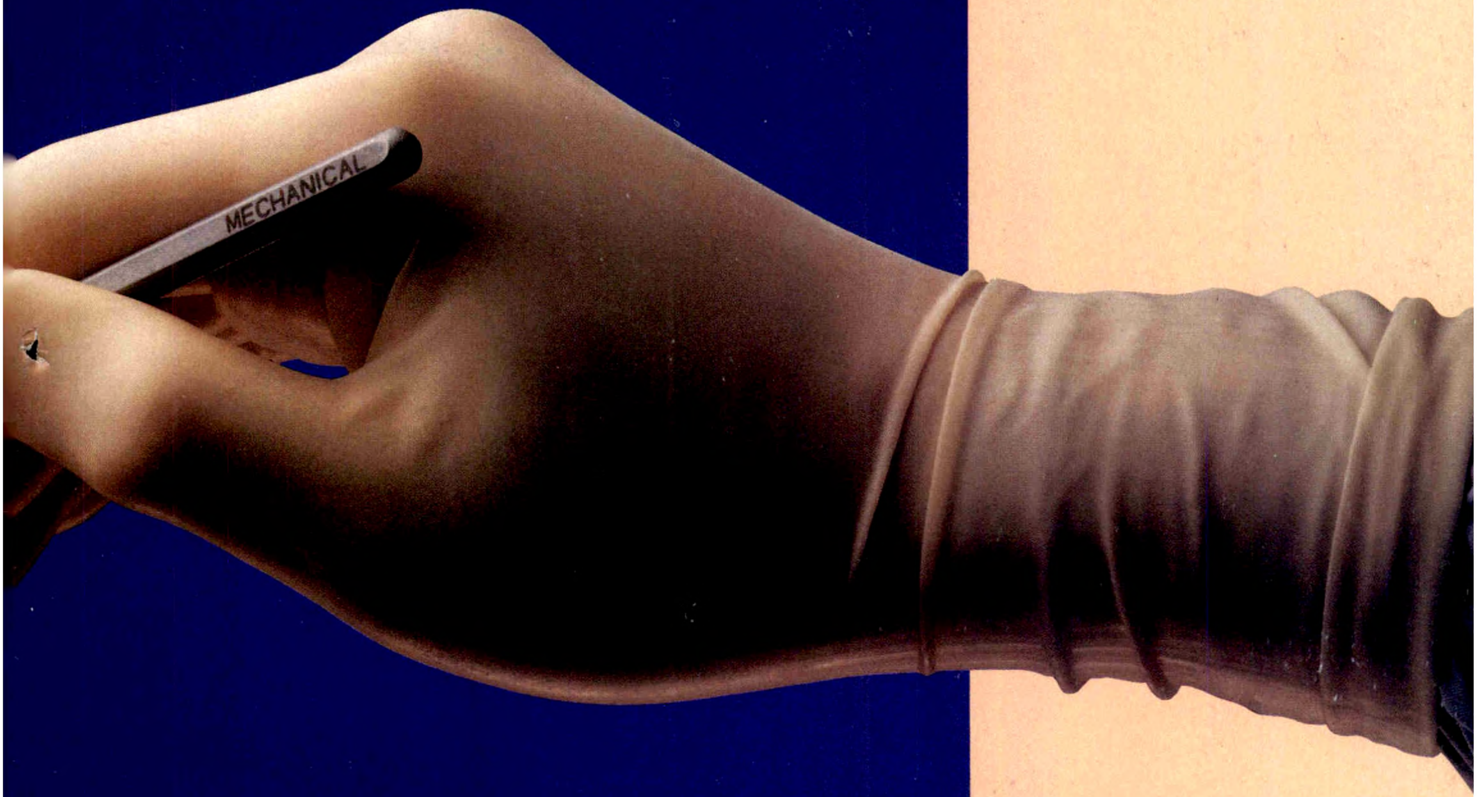
Your Flexible Solution fo

Now you can set the angle you prefer when sizing and inserting the St. Jude Medical® mechanical heart valve. These flexible sizer and holder handles are useful in patients where exposure of the mitral valve is difficult or in patients who have had previous heart surgery.

Steam sterilization straightens the nickle/titanium handles and relieves internal stresses. This increases the useful life of the instruments. Rings and handles are packaged in an autoclavable tray.

For a hands-on demonstration of the Model 903 Bendable Sizer/Valve Holder Set, contact your St. Jude Medical representative. *We're listening and responding. Let us know your needs.*

Inflexible Chests



ST. JUDE MEDICAL

St. Jude Medical, Inc.
One Lillehei Plaza
St. Paul, Minnesota
55117 USA

Telephone (800) 328-9634 or (612) 483-2000
Telex 298453, FAX (612) 482-8318

St. Jude Medical® is a trademark of St. Jude Medical, Inc.

Refer to the physician's manual provided with each device for detailed instructions for use, warnings, precautions and possible adverse device effects. Caution: U.S FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN. © 1989 by St. Jude Medical, Inc. Printed in U.S.A., U.S. Pat. #4,276,658, SP241-01A, 7/89

Continued from page A-9

Unusual Complication of Temporary Pacing Wires in Children 769

Joe W. R. Bolton, MD, and John E. Mayer, Jr, MD

Aneurysm of Coronary Arteriovenous Fistula Presenting as a Calcified Mediastinal Mass 771

Yutaka Okita, MD, Shigehito Miki, MD, Kenji Kusuhara, MD, Yuichi Ueda, MD, Takafumi Tahata, MD, Tetsuro Sakai, MD, Akitoshi Tatsumi, MD, and Morihisa Kitano, MD

Bilateral Elastofibroma Dorsi 774

Hans-Günther Machens, MD, Ruth Mechtersheimer, MD, Ulrich Göhring, MD, and Peter N. Schlag, MD, PhD

Double-Lung Transplantation Using Donor Lungs With a Right Tracheal Bronchus 777

Pierre Y. Brichon, MD, Dominique Blin, MD, Ignacio Perez, MD, Christophe Pison, MD, François Blanc-Jouvan, MD, Isabelle Pin, MD, Didier Barnoud, MD, Elisabeth Brambilla, MD, and René Latreille, MD

Surgical Management of Left Coronary Artery Ostial Atresia and Supravalvar Aortic Stenosis 779

Eliot R. Rosenkranz, MD, Daniel J. Murphy, Jr, MD, and Delos M. Cosgrove III, MD

Hyperbaric Oxygen: Value in Management of Nonhealing Saphenectomy Wounds 782

Michael D. Horowitz, MD, Carmen G. Portogues, PA, Luis A. Matos, MD, and Robert W. McGowan III, PA

Pericardial Repair of a Tracheal Laceration During Transhiatal Esophagectomy 784

Lyall A. Gorenstein, MD, James G. Abel, MD, and G. Alexander Patterson, MD

How to Do It

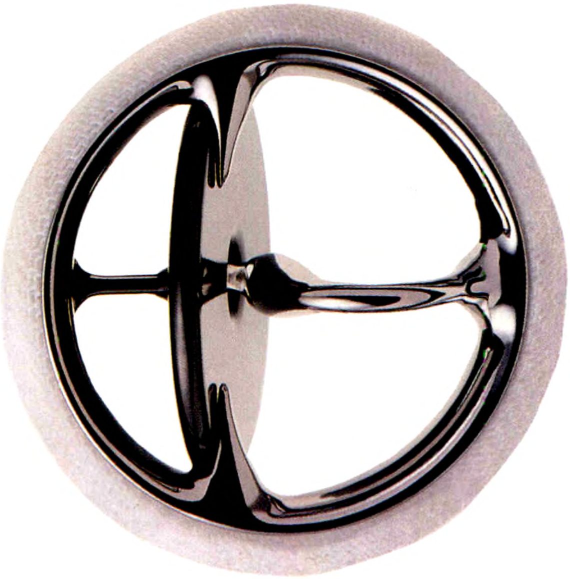
Limited Vertical Skin Incision for Median Sternotomy 787

Shoh Tatebe, MD, Shoji Eguchi, MD, Haruo Miyamura, MD, Satoshi Nakazawa, MD, Hiroshi Watanabe, MD, Masa-aki Sugawara, MD, Jun-ichi Hayashi, MD, Kazutoshi Date, MD, and Satoru Nakagawa, MD

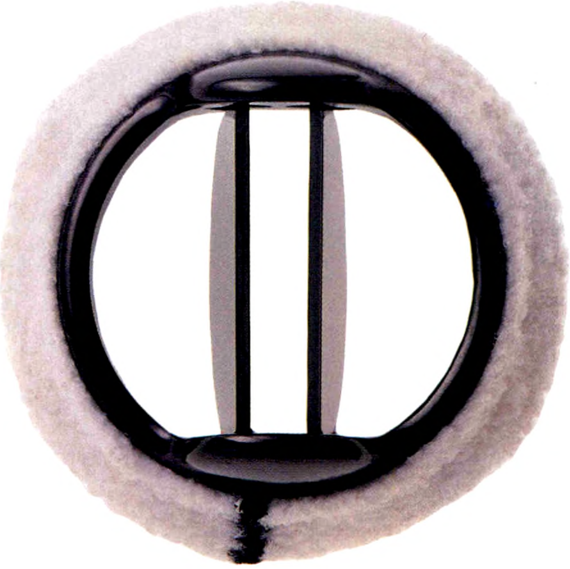
Directed Atraumatic Coronary Sinus Cannulation for Retrograde Cardioplegia Administration 789

Gabriel S. Aldea, MD, Gilbert Connelly, MD, James D. Fonger, MD, Dusan Dobnik, MD, and Richard J. Shemin, MD

continued on page A-16



**MEDTRONIC HALL™
20MM VALVE**



**ST. JUDE MEDICAL
19MM VALVE**

	MANUFACTURER'S STATED SIZE (mm)	TISSUE ANNULUS DIAMETER[1] (mm)	INTERNAL ORIFICE AREA (cm²)	EFFECTIVE ORIFICE AREA[2]* (cm²)	MEAN SYSTOLIC TRANSVALVULAR GRADIENT[2]* (mmHg)
MEDTRONIC HALL™	20	20.08 ± 0.11	2.01	1.74	14.4
ST. JUDE MEDICAL	19	19.76 ± 0.40	1.63▲	1.21	28.4

[1] Data on file, Medtronic, Inc.
▲ St. Jude Medical Physician's Reference Manual.
[2] Data on file, collected by catheter pulse duplication, provided by independent consultant to Medtronic, Inc.
* At a cardiac output of 5 l/min and heart rate of 70 bpm.

MEDTRONIC HALL™
20MM VALVE

© Medtronic, Inc., 1991
All rights reserved

Medtronic

Continued from page A-12

Bilateral Anterior Thoracotomy for Automatic Implantable Cardioverter Defibrillator Placement in Patients With Previous Sternotomy 791

Shreekanth V. Karwande, MD, and John R. Rowles, MD

New Side-Holed Sheath for Intraaortic Balloon Pumping to Maintain Limb Perfusion 794

Hisashi Satoh, MD, Tohru Kobayashi, MD, Taizou Hiraishi, MD, Makoto Sakurai, MD, Yoshiyuki Fudemoto, MD, Mitsunori Kaneko, MD, Susumu Nakano, MD, and Hikaru Matsuda, MD

New Surgical Technique for Type B Aortic Interruption 797

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Fadel Al-Fadley, FRCP(C), Zohair Al-Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

Current Review

Video-Assisted Thoracic Surgery: Basic Technical Concepts and Intercostal Approach Strategies 800

Rodney J. Landreneau, MD, Michael J. Mack, MD, Stephen R. Hazelrigg, MD, Robert D. Dowling, MD, Tea E. Acuff, MD, Mitchell J. Magee, MD, and Peter F. Ferson, MD

Update

Chemoradiation Therapy and Resection for Carcinoma of the Esophagus: Short-term Results 808

Edward F. Parker, MD

Correspondence

Esophageal Perforation 809

Safuh Attar, MD

Reply

William G. Jones II, MD, and Robert J. Ginsberg, MD

Ross' First Homograft Replacement of the Aortic Valve 809

Alfred J. Gunning, FRCS

Reply

Richard A. Hopkins, MD

Reply

Donald Ross, FRCS

continued on page A-20

Pulsatile centrifugal flow is now an option

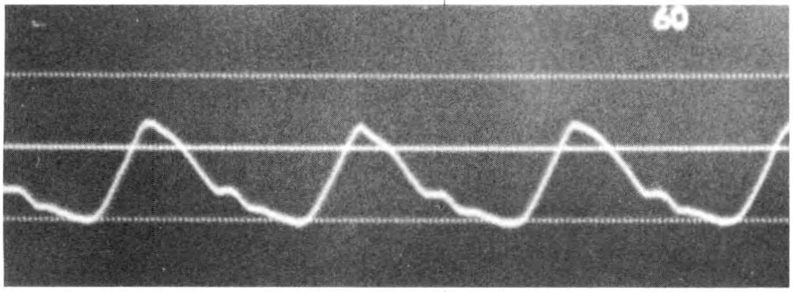
> *"Following a million years of evolutionary adaptation it seems teleologically reasonable to suppose that the ideal aortic waveform will be similar to that generated by the natural left ventricle."*[1]

The most obvious goal of cardiopulmonary bypass (CPB) is to maintain cardiac and respiratory function in a near-physiologic manner. While continuous flow has been used successfully in thousands of open heart procedures, advocates of pulsatile flow claim that it more closely approximates the activity of a normal heart. Now pulsatile flow is available even when using a centrifugal pump.

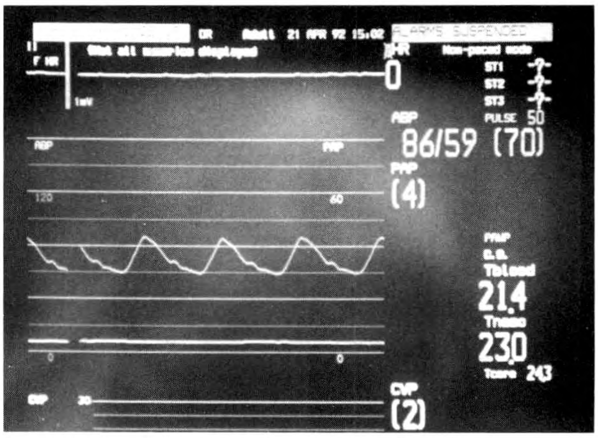
A recent study of 50 patients documented some physiologic benefits for the 25 who were supported with pulsatile flow using the Sarns centrifugal pump during bypass.[2] (Non-pulsatile flow was provided by a conventional roller pump.)

Patients in the pulsatile flow group

- Required much smaller doses of sodium nitroprusside to keep systemic vascular resistance within physiologic limits
- Extracted more oxygen during rewarming
- Had no postoperative decrease in white blood cell count (after correction for changes in hematocrit).



The lower doses of sodium nitroprusside allowed for "faster rewarming with less, possibly toxic, pharmacologic intervention."[2] The authors theorized that the higher oxygen consumption resulted from better microcirculation during CPB. They added, "Our study suggests that centrifugal pumps should have a mechanism to deliver pulsatile flow."[2]

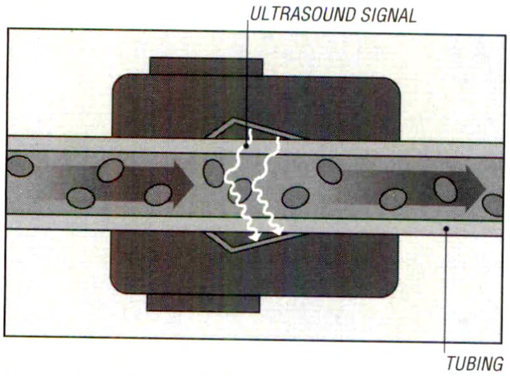


◄A recognizable arterial waveform is generated by the Sarns™ centrifugal pump during CPB for a CABG X 3.[3]

Non-invasive, digitally precise flow sensing

The Delphin sensor employs digital signal processing (DSP) technology, a convenient and accurate way to determine flow rates. The non-invasive sensor eliminates worries about sensor site contamination or thrombogenesis. The sensor simply clips around the outside of standard 3/8" tubing. Because the sensor is non-invasive, it is also reusable, making it less costly than disposable probes.

The Delphin flow sensor relies on Doppler-based technology, housed in the control module, which converts raw sensor data into precise digital readouts. Readings are displayed over a range from .05 to 9.9 L/min. DSP minimizes inaccuracies caused by clinical variables such as blood and tube temperature, tube stiffness, blood viscosity, hematocrit, and pump vibration.

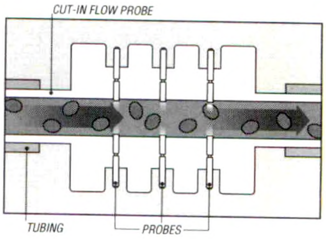


Non-invasive Delphin sensor

Flow sensor data is converted into accurate readouts by digital signal processing (DSP) housed in the Delphin control module.

Invasive flow probes

The electromagnetic flow probes found on other pumps are affected by slight changes in hematocrit and temperature.[4] *Specifically, as hematocrit increases, the electromagnetic flow measurement decreases, and at lower hematocrits the measured flow rate is erroneously elevated.*



Quick set-up

The Delphin sensor requires no time-consuming warm-up or sensor zeroing, and Delphin sensors are interchangeable with any Delphin II console. The operator enters in the sensor's calibration number the first time it is used with a specific console. There is no need to re-enter the calibration number unless the sensor is moved to another console. The time savings become especially critical in emergency situations.

For more information about the Sarns Delphin II centrifugal system and pulsatile flow, call **800/521-2818**. Or write Sarns, 3M Health Care, 6200 Jackson Road, Ann Arbor, MI 48103.

Footnotes

[1] Wright G. The hydraulic power outputs of pulsatile and nonpulsatile cardiopulmonary bypass pumps. *Perfusion*. 1988;3:251-262.

[2] Driessen JJ, Fransen G, Rondelez L, et al. Comparison of the standard roller pump and a pulsatile centrifugal pump for extracorporeal circulation during routine coronary artery bypass grafting. *Perfusion*. 1991;6:303-311.

[3] Photo courtesy of Steven Demos, MD, Ron Duff, CCP, and Leon Conklin, CCP, and the Heart Team at Mercy Medical Center in Muskegon, Michigan.

[4] Akers T, Bolen G, Gomez J, et al. In vitro comparison of ECC blood flow measurement techniques. Proceedings of the American Academy of Cardiovascular Perfusion, 1990.

Sarns and Delphin are trademarks of 3M.

©1992 3M 36USC380

Innovation working for you™

3M

Worldwide Sponsor 1992 Olympic Games

THE FIRST INTERNATIONAL SYMPOSIUM OF

THORACOSCOPIC SURGERY

JANUARY 22-23, 1993 • SAN ANTONIO, TEXAS

PROGRAM DIRECTOR

Michael Mack, M.D.
Humana Hospital-
Medical City Dallas

IMMEDIATELY PRIOR TO STS

THE FIRST INTERNATIONAL SYMPOSIUM OF THORACOSCOPIC SURGERY

JANUARY 22-23, 1993

PLEASE PRINT OR TYPE

☐ Send Information
☐ Register Me

Name: First Last M.D., Prof., R.N. Companion

Mailing Address Hospital

City State Zip Country

Telephone Fax Specialty

Mail to: PROMEDICA INTERNATIONAL • 620 Newport Center Drive, Suite 575 • Newport Beach, CA 92660 • USA
Contact: Margo Irr • TEL (714) 640-5870 Ext 28 • FAX (714) 759-6911

Continued from page A-16

Continuous Normothermic Blood Cardioplegia: Simplified Delivery Circuit 810

Ponangi V. Satyanarayana, MS, MCh, Podila Sita Rama Rao, MS, MCh,
Kesavaram Madhusudhana Rao, BSc, CCP, Alluru Sarath Chandra, MS,
Kanchumarthi Sudhakar Rao, MS, and Karri Venkat Reddy, MS

Thromboelastogram and Postoperative Hemorrhage 810

Bruce D. Spiess, MD

Kenneth J. Tuman, MD, Robert J. McCarthy, PharmD, and Anthony D. Ivankovich, MD

Paul G. Martin, BSc, Ferenc Horkay, MD, Nirmal K. Gupta, MCh, and
Duncan R. Walker, FRCS

Reply

Chung-Yuan Lin, MD, and Jian-Sheng Wang, MD

Palliative Intubation for Dysphagia 813

Lewis Wetstein, MD

Reply

Theodore K. Liakakos, MD, Sunil K. Ohri, FRCS, Edward R. Townsend, FRCS, and
S. William Fountain, FRCS

The Blue Man Phenomenon 814

Ian M. Mitchell, FRCS, Nigel R. Saunders, FRCS, Robert D. Paton, PhD, and
Robert W. Logan, FRCP(Glasg)

Minimal Hemodilution and Optimal Potassium Use During Normothermic Aerobic Arrest 815

Daniel Le Houerou, MD, Ajoy I. Singh, MD, Mauro Romano, MD, Victor Martin, MD,
and Arrigo Lessana, MD

Rapid Transfusion After Aortic Decannulation 816

Jose M. Bernal, MD, Jose M. Rabasa, MD, and Jose M. Revuelta, MD

Review of Recent Books

Mediastinal Surgery, edited by Thomas W. Shields, MD 781

James L. Nielsen, MD

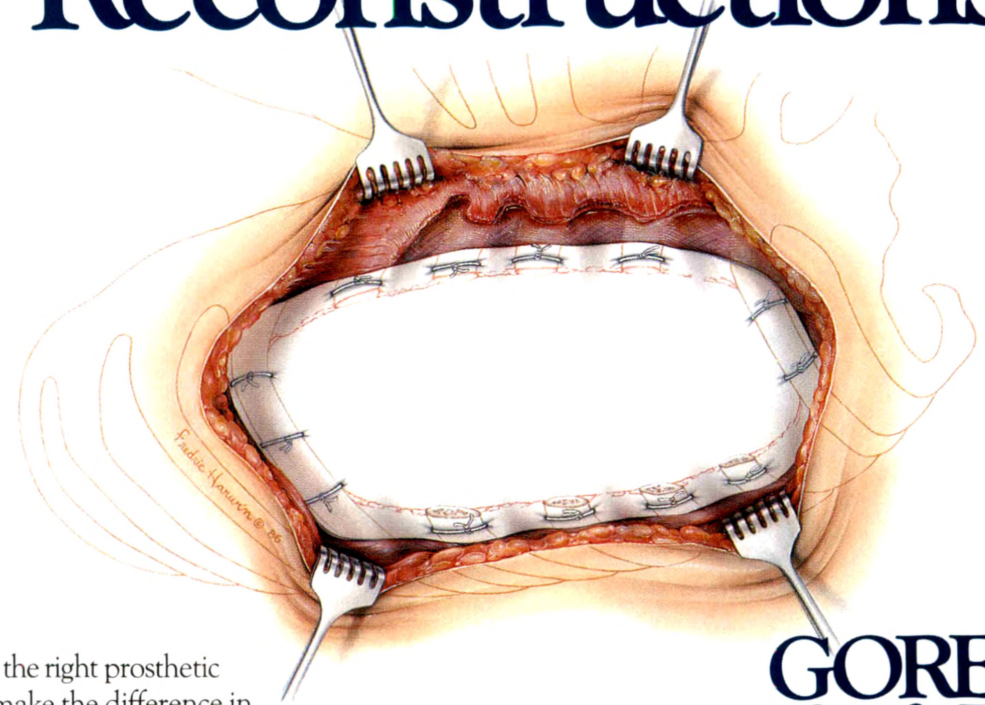
Announcements

Forthcoming Articles A-26

Information for Authors A-27, 28

continued on page A-22

Meeting the surgical challenge: Chest Wall Reconstructions.



Choosing the right prosthetic material can make the difference in successful chest wall reconstructions. Thoracic surgeons are finding that the GORE-TEX Soft Tissue Patch makes that difference.

The Difference

A key advantage of the Soft Tissue Patch in chest wall reconstructions is its microporous structure that inhibits the passage of fluid.[1] This helps in re-establishing pulmonary function by restricting air leakage and preventing the transfer of pleural fluid across the chest wall.

The material's high, balanced strength

- allows the tension needed for a firm reconstruction that minimizes paradoxical wall movement and
- provides dependable suture retention.

Yet, the material remains soft and highly conformable allowing

- an ease of handling and
- less irritation to surrounding tissues.

Tissue ingrowth is encouraged by the microporous structure of this unique material. It has been shown to resist the spread of infection, be treatable in its presence and, result in a significantly lower incidence of adhesion formation.[2] It combines strength with softness to provide unmatched performance and superior handling.

For more information, return the coupon or call, 800/638-4804.

1. Pairolero PC, Arnold PG. Chest wall tumors: experience with 100 consecutive patients. Journal of Thoracic and Cardiovascular Surgery 90:367-372, 1985.
2. Brown GL, et al. Comparison of prosthetic materials for abdominal wall reconstruction in the presence of contamination and infection. Annals of Surgery 201(6):705-711, 1985.

GORE-TEX™ Soft Tissue Patch

☐ Please send further information on the GORE-TEX™ Soft Tissue Patch, including the cited articles.

☐ Please have your sales representative call for an appointment.

☐ Please arrange to send a free clinical sample of the GORE-TEX™ Soft Tissue Patch.

Name

Address

City

State Zip

Surgical Specialty

Phone

Hospital Affiliation

W.L. Gore & Associates, Inc.
P.O. Box 1220, Route 213 North
Elkton, MD 21921

AOTS-10-92STP2

GORE

CREATIVE TECHNOLOGIES
WORLDWIDE

GORE-TEX is a trademark of W.L. Gore & Associates, Inc.
© 1987 W. L. Gore & Associates, Inc.

Continued from page A-20

Guidelines for the Submission of Electronic Manuscripts A-29

Events of Interest A-30, 31

Notice From The Society of Thoracic Surgeons 675

Notice From the Southern Thoracic Surgical Association 740

Notice From the American Board of Thoracic Surgery 783, 793

Classified Advertisements A-33, 34, 35

Index to Advertisers A-42

GENERAL INFORMATION *The Annals of Thoracic Surgery* is indexed/abstracted in *Index Medicus, Current Contents/Clinical Practice/Life Sciences, Excerpta Medica, Reference Update*, and *Biological Abstracts*.

Please direct orders for subscriptions, single copies, and back issues; changes of address; and claims for missing issues to: Journals Fulfillment Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Claims for missing issues can be honored only up to 3 months for domestic addresses, 6 months for foreign addresses. Duplicate copies will not be sent to replace ones undelivered through failure to notify Elsevier of change of address.

The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery*, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.

Microfilm copies are available through University Microfilms International, 300 North Zeeb Road, Ann Arbor, MI 48106.

Reprints, except special orders of 100 or more, are available from the authors.

Advertising inquiries should be addressed to: Art Carlucci, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3880).

The publisher assumes no responsibility for any injury and/or damage to persons or property as a matter of products liability, negligence, or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. No suggested test or procedure should be carried out unless, in the reader's judgment, its risk is justified. Because of rapid advances in the medical sciences, we recommend that the independent verification of diagnoses and drug dosages should be made. Discussions, views, and recommendations as to medical procedures, choice of drugs, and drug dosages are the responsibility of the authors.

Although all advertising material is expected to conform to ethical (medical) standards, inclusion in this publication does not constitute a guarantee or endorsement of the quality or value of such product or of the claim made of it by its manufacturer.

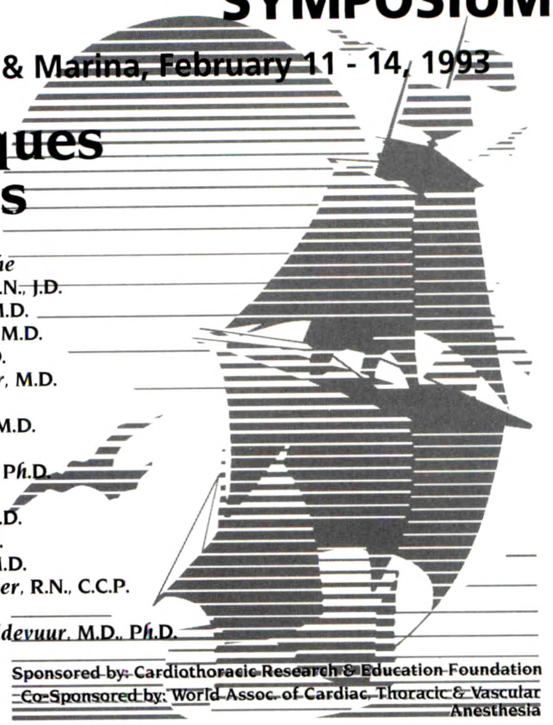
This journal has been registered with the Copyright Clearance Center, Inc. Consent is given for the copying of articles for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition that the copier pay through the Center the per copy fee stated in the code on the first page of each article for copying beyond that permitted by the US Copyright Law. The appropriate fee should be forwarded with a copy of the first page of the article to the Copyright Clearance Center, Inc, 27 Congress Street, Salem, MA 01970. If no code appears on an article, the author has not given broad consent to copy, and permission to copy must be obtained directly from the author. This consent does not extend to other kinds of copying, such as for general distribution, resale, advertising and promotional purposes, or for creating new collective works. All inquiries regarding copyrighted material from this publication, other than reproduction through the Copyright Clearance Center, should be directed to Rights and Permissions Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; (212) 633-3977.

This journal is printed on acid-free paper.

© 1992 by The Society of Thoracic Surgeons

13th Annual SAN DIEGO CARDIOTHORACIC SURGERY SYMPOSIUM

San Diego Marriott Hotel & Marina, February 11 - 14, 1993



Pathophysiology & Techniques of Cardiopulmonary Bypass

Program Director:
Joe R. Utley, M.D.

This course is of interest to all members of the team caring for the cardiac surgery patient, including physicians and surgeons, perfusionists, nurses and nurse anesthesiologists, intensivists, and biomedical health professionals. Continuing education credit will be awarded to physicians, perfusionists, nurses, and CRNAS.

Faculty Includes:

- James A. Alexander, M.D.
- Roy E. Bolles, C.C.P.
- Mark Bruley
- John F. Butterworth, IV, M.D.
- David Cross, M.D.
- Rick Davis, M.D.
- William Edelman
- John Fung, M.D.
- Glenn Gravlee, M.D.
- Steven R. Gundry, MD.
- Carl Hug, M.D.
- W.J. Kolff, M.D.
- Glen Warren Laub, M.D.
- William B. Long, M.D.
- George J. Magovern, Jr. M.D.
- Jack Marlotte
- Dr. Philippe Menacshe
- Kathleen S. Music, R.N., J.D.
- Luis Oppenheimer, M.D.
- A. Thomas Pezzella, M.D.
- Albert J. Pfister, M.D.
- Robert E. Rawitscher, M.D.
- Jeff Riley, B.A.
- Richard M. Satava, M.D.
- Phil Scott, C.C.P.
- George Silvay, M.D., Ph.D.
- Julie A. Swain, M.D.
- Michael Sweeney, M.D.
- Joseph T. Walls, M.D.
- Andrew Wechsler, M.D.
- Mary Hartley Winkler, R.N., C.C.P.
- Allen Willner, Ph.D.
- Prof. Dr. Ch.R.H. Wildevuur, M.D., Ph.D.

The symposium will be conducetd in English with simultaneous translations to German & French.

Sponsored by: Cardiothoracic Research & Education Foundation
Co-Sponsored by: World Assoc. of Cardiac, Thoracic & Vascular Anesthesia

Abstracts will be accepted for presentation until January 1, 1993. For abstract forms or program information including registration and hotel accommodation forms, send a postcard with your name, specialty, and address to:

C.R.E.F. P.O. Box 23220, San Diego, CA 92193 or Fax (619) 541-144 Voice (619) 541-1444

THE MOUNT SINAI MEDICAL CENTER, NEW YORK • Program Director: Randall B. Griepp, M.D.

AORTIC SURGERY SYMPOSIUM III

VIDEO PROCEEDINGS (INCLUDING PANEL DISCUSSIONS)

FACULTY

- Jean Bachet, M.D.
- Hans Borst, M.D.
- Christian Cabrol, M.D.
- Alain Carpentier, M.D., Ph.D.
- Denton Cooley, M.D.
- Joseph Coselli, M.D.
- Joseph N. Cunningham, M.D.
- Arisan M. Ergin, M.D.
- Richard Gorlin, M.D.
- Randall Griepp, M.D.
- Nicholas Kouchoukos, M.D.
- Steven Lansman, M.D.
- Kenneth Mattox, M.D.
- D. Craig Miller, M.D.

Aortic Surgery Symposium IV, April 22-23, 1994, New York, New York

PLEASE CHECK

☐ Session I	$ 100
☐ Session II	$ 100
☐ Session III	$ 100
☐ Session IV	$ 100
☐ All four sessions (save $50)	$ 350
* Plus shipping & handling	
U.S. - Ground	$ 15
Canada - Ground	$ 20
Europe - Air	$ 75
State Sales Tax (CA only)	$ ___
Total Order	$ ___

ALL FEES IN U.S. DOLLARS DRAWN ON U.S. BANKS
All tapes in NTSE format

☐ Check enclosed ☐ VISA/MasterCard ☐ AmEx

Credit Card # ____________________

Expiration Date ____________________

AORTIC SURGERY SYMPOSIUM III • VIDEO ORDER FORM

I agree not to reproduce these videos outside my institute or present this material without prior written permission from Dr. Lansman.

Signature____________________ Date ____________

PLEASE PRINT OR TYPE

Name:
First Last M.D., Prof., R.N.

Shipping Address

City State Zip Country

Telephone Fax

Signature for Credit Card

Mail to: PROMEDICA INTERNATIONAL • 620 Newport Center Drive, Suite 575 • Newport Beach, CA 92660 • USA
Contact: Lisa Turnbull • TEL (714) 640-5870 Ext 20 • FAX (714) 759-6911

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Editor

Thomas B. Ferguson, MD, St. Louis, MO

Herbert Sloan, MD, Editor 1969–1984
John D. Steele, MD, Editor 1964–1969

Associate Editors

John R. Benfield, MD, Sacramento, CA
Anthony R. C. Dobell, MD, Montreal, Canada
Marvin M. Kirsh, MD, Ann Arbor, MI
Hassan Najafi, MD, Chicago, IL
J. Kent Trinkle, MD, Book Review Editor
University of Texas Health Science Center
7703 Floyd Curl Drive, San Antonio, TX 78284-7841

Editorial Board

Hendrick B. Barner, MD, New Hyde Park, NY
Harvey W. Bender, Jr, MD, Nashville, TN
Ray Chu-Jeng Chiu, MD, PhD, Montreal, Canada
Lawrence H. Cohn, MD, Boston, MA
Jack G. Copeland III, MD, Tucson, AZ
Delos M. Cosgrove III, MD, Cleveland, OH
Timothy J. Gardner, MD, Baltimore, MD
William A. Gay, Jr, MD, Salt Lake City, UT
Robert A. Guyton, MD, Atlanta, GA
Clement A. Hiebert, MD, Windham, ME
Takashi Iwa, MD, Kanazawa, Japan
Robert B. Karp, MD, Chicago, IL
James E. Lowe, MD, Durham, NC
Douglas J. Mathisen, MD, Boston, MA
Philippe Menasché, MD, PhD, Paris, France
William I. Norwood, Jr, MD, Philadelphia, PA
John L. Ochsner, MD, New Orleans, LA
Mark B. Orringer, MD, Ann Arbor, MI
Peter C. Pairolero, MD, Rochester, MN
Richard M. Peters, MD, Palo Alto, CA
W. Gerald Rainer, MD, Denver, CO
Charles L. Roper, MD, St. Louis, MO
Thomas W. Shields, MD, Chicago, IL
Jaroslav Stark, MD, London, England
Larry W. Stephenson, MD, Detroit, MI
Kenneth M. Taylor, MD, London, England

Administrative Editor

Carol L. Blasberg, St. Louis, MO

Editorial Office

The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

To provide a place for ALL thoracic surgeons to relate experiences which will help other practicing thoracic surgeons give better patient care.
Herbert Sloan, MD

The Society of Thoracic Surgeons

Officers

President	Vincent L. Gott, MD
Vice President	Denton A. Cooley, MD
Secretary	Richard P. Anderson, MD
Treasurer	Nicholas T. Kouchoukos, MD
Editor	Thomas B. Ferguson, MD
Historian	W. Gerald Rainer, MD

Councillors at Large

Leonard L. Bailey, MD
James L. Cox, MD
H. Storm Floten, MD
Timothy J. Gardner, MD
Robert J. Ginsberg, MD
Peter C. Pairolero, MD

Business Manager
Walter G. Purcell

Southern Thoracic Surgical Association

Officers

President	William A. Cook, MD
President-Elect	Gordon F. Murray, MD
Vice President	Joseph I. Miller, Jr, MD
Secretary-Treasurer	Hendrick B. Barner, MD
Editor	Thomas B. Ferguson, MD
Historian	Hawley H. Seiler, MD

Council

Robert M. Sade, MD
Chairman
William C. Alford, Jr, MD
Hendrick B. Barner, MD
William A. Cook, MD
Timothy J. Gardner, MD
Joseph I. Miller, Jr, MD
Gordon F. Murray, MD
D. Glenn Pennington, MD
William F. Sasser, MD
Thomas B. Ferguson, MD (Ex Officio)

Business Manager
Walter G. Purcell

For information about either organization, contact either The Society of Thoracic Surgeons or the Southern Thoracic Surgical Association at 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

FORTHCOMING ARTICLES

Original Articles

■ Acute Rejection of Lung Allografts With Various Immunosuppressive Protocols

Bartley P. Griffith, MD, Robert L. Hardesty, MD, John M. Armitage, MD, Robert L. Kormos, MD, Gary C. Marrone, MD, Steve Duncan, MD, Irvin Paradis, MD, James Dauber, MD, Samuel Yousem, MD, and Penny Williams, MD

■ Cardiac Retransplantation: A Viable Option?

Shreekanth V. Karwande, MD, R. Douglas Ensley, MD, Dale G. Renlund, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, Donald B. Doty, MD, M. Elizabeth Hammond, MD, John D. Marks, PE, and The Registry of the International Society for Heart and Lung Transplantation

■ Clinical Manifestation of Mediastinal Fibrosis and Histoplasmosis

Douglas J. Mathisen, MD, and Hermes C. Grillo, MD

■ Coarctation of the Aorta in Infants: Does the Aortic Arch Grow After Repair?

John L. Myers, MD, Brian A. McConnell, BS, and John A. Waldhausen, MD

■ Coronary Sinus Injuries During Retrograde Continuous Normothermic Blood Cardioplegia

Anthony L. Panos, MD, Imtiaz S. Ali, MD, Peter L. Birnbaum, MD, Carlos A. M. Barrozo, MD, Owayed Al-Nowaiser, MD, and Tomas A. Salerno, MD

■ Cryopreserved Allograft Veins as Alternative Coronary Artery Bypass Conduits: Early Phase Results

Glenn W. Laub, MD, S. Muralidharan, MD, Robert Clancy, RN, W. Jay Eldredge, MD, Chao Chen, PhD, Mark S. Adkins, MD, Javier Fernandez, MD, William A. Anderson, MD, and Lynn B. McGrath, MD

■ Extrapleural Pneumonectomy in the Treatment of Malignant Pleural Mesothelioma

David J. Sugarbaker, MD, Steven J. Mentzer, MD, and Gary Strauss, MD

■ Intrathecal Perfusion of an Oxygenated Perfluorocarbon Prevents Paraplegia After Aortic Occlusion

Robert E. Maughan, MD, Chittur Mohan, MD, Ira M. Nathan, PhD, Enrico Ascer, MD, Peter Damiani, BS, Israel J. Jacobowitz, MD, Joseph N. Cunningham, Jr, MD, and Corrado P. Marini, MD

■ Late Results of Operation for Ventricular Tachycardia

Lynda L. Mickleborough, MD, Shun-ichi Mizuno, MD, Eugene Downar, MD, and Gordon C. Gray, BSc

■ Long-Term Effect of Total Fundoplication on the Myotomized Esophagus

Philippe Topart, MD, Claude Deschamps, MD, Raymond Taillefer, MD, and André Duranceau, MD

■ Postcardiotomy Centrifugal Mechanical Ventricular Support

Leonard A. R. Golding, MD, Ray D. Crouch, MD, Robert W. Stewart, MD, Roberto Novoa, MD, Bruce W. Lytle, MD, Patrick M. McCarthy, MD, Paul C. Taylor, MD, Floyd D. Loop, MD, and Delos M. Cosgrove III, MD

■ Risk Analysis of Operative Intervention for Failed Coronary Angioplasty

A. Michael Borkon, MD, Trent L. Failing, MD, Jeffrey M. Piehler, MD, Duncan A. Killen, MD, Marcia L. Hoskins, MD, and William A. Reed, MD

Case Reports

■ Aneurysm of the Ascending Aorta After Cardiac Transplantation

Jean-Olivier Defraigne, MD, Olivier Vahdat, MD, Jean-Paul Lavigne, MD, Jean-Claude Demoulin, MD, PhD, and Raymond Limet, MD, PhD

■ True Aneurysm of the Saphenous Vein Graft Stump Associated With Coronary Artery Bypass Grafting in a Cardiac Transplant Patient

Robert T. Baldwin, MD, Tomas Klima, MD, O. Howard Frazier, MD, James Lonquist, MD, and Branislav Radovancevic, MD

How to Do It

■ New Surgical Technique for Total-Defect Aortopulmonary Window

Osamu Matsuki, MD, Toshikatsu Yagihara, MD, Fumio Yamamoto, MD, Kyoichi Nishigaki, MD, Hideki Uemura, MD, and Yasunara Kawashima, MD

■ Permanent Pacemaker Implantation in Premature Infants Less Than 2,000 Grams of Body Weight

Mikio Ohmi, MD, Motohisa Tofukuji, MD, Kaori Sato, MD, Takahiko Nakame, MD, Naoshi Sato, MD, Kiyoshi Haneda, MD, and Hitoshi Mohri, MD

Classics in Thoracic Surgery

■ Clarence Crafoord and the First Successful Resection of a Cardiac Myxoma

W. Randolph Chitwood, Jr, MD

THE ANNALS OF THORACIC SURGERY
INFORMATION FOR AUTHORS

Thomas B. Ferguson, MD
Editor, *The Annals of Thoracic Surgery*
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

The Annals of Thoracic Surgery publishes original papers on topics in thoracic and cardiovascular surgery. Also featured are case reports, "how to do it" articles, classics in thoracic surgery, collective and current reviews, correspondence, and book reviews. All manuscripts, correspondence, and editorial business should be sent to the above address. Guidelines for collective and current reviews are available on request.

If a manuscript is accepted for publication, certain conditions must be agreed to by all authors. These include statements regarding conflict of interest, scientific responsibility, exclusive publication, and assignment of copyright. Elsevier Science Publishing Co, Inc, will maintain records of copyright for The Society. No part of the published material may be reproduced elsewhere without written permission from the publisher.

Because of escalating postage costs, manuscripts and illustrations will not routinely be returned to the authors. The editorial office will be responsible for proper disposal of the manuscripts so that confidentiality is preserved. Manuscripts and illustrations will be returned only if requested and a self-addressed stamped (US postage) envelope provided.

Checklist

The following checklist is provided for the author's convenience. Please utilize this list to make certain the manuscript is complete when submitted. Incomplete manuscripts cannot be accepted for editorial review.

General

- ☐ Submit original and *two* duplicate manuscripts (including three clearly separated and labeled sets of illustrations). Retain a fourth complete set as insurance against loss in the mail.
- ☐ Type manuscript double-spaced throughout (including title page, abstract, text, references, tables, and legends) on one side only on 22 × 28 cm (8½ × 11 inch) opaque bond paper with 3 cm (1¼ inch) margins all around. *This also applies to correspondence.* Type the last name of the first author in the upper right-hand corner of each page, including the title page.
- ☐ Arrange manuscript as follows: (1) title page, (2) abstract, (3) text, (4) references, (5) tables, and (6) legends. Number pages consecutively, beginning with the title page as page 1 and ending with the legend page.
- ☐ A manuscript for an *original article* ordinarily should not exceed 26 double-spaced typewritten pages, and should be proportionally shorter the more illustrations and tables that are included.
- ☐ The *text* for case reports should be *no more* than 4 double-spaced typewritten pages. If tables or illustrations are included, the text must be reduced. The text for a "how to do it" article should be even briefer, but with detailed illustrative material. Case reports and "how to do it" articles that exceed the allowable length will not be considered for publication.
- ☐ Referencing should be selective and pertain directly to the work being reported. Except in collective and current reviews, comprehensive listings serve no useful purpose and utilize valuable space. As a general guide, original articles should have no more than 20 references; case reports, 8 references; and "how to do it" articles, 5 references.

Title Page

- ☐ Give the paper as short a title as possible. Also submit a short title of 3 or 4 words to be used as a running head. Include only the names of the authors directly affiliated with the work, stating for each the single highest academic degree. Include the name and location of no more than two institutional affiliations.
- ☐ If the paper has been or is to be presented at the annual meeting of The Society of Thoracic Surgeons, the Southern Thoracic Surgical Association, or another scientific organization, provide a footnote giving the name, location, and dates of the meeting.
- ☐ At the bottom of the page, type "Address reprint requests to Dr . . ." followed by the last name, exact postal address with zip code, *telephone number, and FAX number* of the author to whom communications, proofs, and requests for reprints should be sent.

Abstracts

- ☐ Provide an abstract *no longer than 175 words* for an original article. Abstracts for case reports and "how to do it" articles should be shorter (50 to 75 words). An abstract must accompany *every* contribution, except for letters to the editor. Include several (3 to 5) keywords to assist in cross-indexing the article.

Text

- ☐ Generally, the text should be organized as follows: Introduction, Material and Methods, Results, and Comment.
- ☐ *Cite references, illustrations, and tables in numerical order* in the text. (Order of mention in text determines the number given to each.)
- ☐ Spell out, or define in parentheses, all abbreviations, even if they are commonly employed.
- ☐ Give all measurements and weights in *Système International (SI) units.* See "SI Unit Implementation—the Next Step" (JAMA 1988;260:73–6).
- ☐ For statistical nomenclature and data analysis, follow the "Guidelines for Data Reporting and Nomenclature" published in *The Annals of Thoracic Surgery* (1988;46:260–1) and found in the program book for the annual meeting of The Society of Thoracic Surgeons.
- ☐ Type footnotes at the bottom of the manuscript page on which they are cited. Credit suppliers of drugs, equipment, and other material described at length in the paper in footnotes, giving company name and location.
- ☐ Type acknowledgments, including complete grant or subsidy information, at the end of the text before the references.

References

- ☐ Identify references in the text using arabic numerals in parentheses on the line. Do not cite personal communications, manuscripts in preparation, and other unpublished data in the reference list. They may be mentioned in the text in parentheses.
- ☐ Type references double-spaced on a separate sheet. *Number consecutively in the order in which they are mentioned in the text.*
- ☐ Journal references should provide *inclusive* page numbers; book references should cite *specific* page numbers.
- ☐ Double-check references for accuracy, completeness, and nonduplication.

(Continued)

© 1992 by The Society of Thoracic Surgeons

P. 24824

☐ Abbreviations of journals should conform to those used in *Index Medicus*. The style and punctuation of the references should follow the formats outlined below:

Journal Article

8. Grillo HC, Suen HC, Mathisen DJ, Wain JC. Resectional management of thyroid carcinoma invading the airway. Ann Thorac Surg 1992;54:3–10.

(List *all* authors if 6 or fewer; otherwise list first 3 and add "et al.")

Chapter in Book

12. Vouhé PR. Transplantation of thoracic organs in children. In: Fallis JC, Filler RM, Lemoine G, eds. Pediatric thoracic surgery. New York: Elsevier, 1991:319–29.

Book (Personal Authors or Editors)

18. Shields TW, ed. Mediastinal surgery. Philadelphia: Lea & Febiger, 1991:1–10.

Tables

☐ Tables should be typewritten *double-spaced* on separate sheets, each with a table number (arabic) and title above the table and explanatory notes and legends below. Provide a key in alphabetical order to each table to identify all abbreviations used; this key should be placed below any explanatory notes.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published table(s).

☐ Tables should be self-explanatory, and the data should not be duplicated in the text or illustrations. If a table provides redundant information, it will be deleted.

Legends

☐ Type legends double-spaced on a single sheet. Numbers should be arabic and correspond to the order in which the illustrations occur in the text. Identify (in alphabetical order) all abbreviations appearing in the illustrations at the end of each legend. Give the type of stain and magnification power for all photomicrographs.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published illustration(s).

☐ Enclose signed releases for recognizable (unmasked) photographs of human beings.

Illustrations

☐ Submit *triplicate* sets, each set in its own envelope, of *unmounted* and untrimmed black and white professionally prepared glossy prints. Components of the same illustration (eg, parts A and B) should be submitted separately. Photographs, rather than original art or photocopies, should be provided. All lettering should be done professionally and should be of adequate size to retain clarity after reduction (*final* lettering size in print should be 1.5 mm high). Illustrations will be reproduced at a width of one column (8.25 cm, 3¼ inches) or two columns (17.15 cm, 6¾ inches), or at an intermediate width ranging from 10.16 to 12.07 cm (4 to 4¾ inches).

☐ Many computer-generated illustrations are unsatisfactory for reproduction and should be professionally redrawn. Roentgenogram reproductions should be no smaller than 13 × 18 cm (5 × 7 inches).

☐ Place the first author's last name, the figure number, and an arrow indicating the *top* on a gummed label on the back of each illustration.

☐ If color illustrations are to be considered for publication, submit *both* positive 35-mm transparencies and color prints. Part of the printing costs for color illustrations will be borne by *The Annals*; however, the author must be prepared to pay $1,150 for the first color illustration on each page and $250 for every additional color illustration on the same page.

Human Investigation

☐ Include the date of approval by the local institutional human research committee or the ethical guidelines that were followed by the investigators in the Material and Methods section of the manuscript.

Humane Animal Care

☐ The Material and Methods section must contain a statement assuring that all animals have received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

Conflict of Interest

The Annals expects authors to disclose any commercial association that might pose a conflict of interest in connection with this manuscript. All funding sources supporting the work should be acknowledged in a footnote. Institutional or corporate affiliations of the authors that might constitute a conflict should be brought to the attention of the Editor.

Scientific Responsibility Statement

Before publication of an accepted manuscript, each author will be required to certify that he or she has participated sufficiently in the work to take responsibility for a meaningful share of the content of the manuscript, and that this participation included:

(a) conception or design of the experiment(s), or collection and analysis or interpretation of data;

(b) drafting the manuscript or revising its intellectual content; and

(c) approval of the final version of the manuscript to be published.

Exclusive Publication Statement

I certify that none of the material in this manuscript has been published previously, and that none of this material is currently under consideration for publication elsewhere. This includes symposia, transactions, books, articles published by invitation, and preliminary publications of any kind except an abstract of 400 words or fewer.

____

(Author's Signature)

Guidelines for the Submission of Electronic Manuscripts

☐ Please note that only the final accepted revision of a manuscript should be submitted as an electronic file. If you are planning to submit a manuscript in this format, please check box.

I. *Keyboarding of Manuscripts*

1) Our equipment can handle the following programs (any version) in their "native" format:

IBM Compatible

DisplayWrite
Executive Writer
Leading Edge
MicroSoft Word
Multimate
Office Writer
PC Write
PFS: Write
PFS: Professional
Q & A Write
Samna
Spellbinder
Volkswriter
WordPerfect
WordStar
WordStar 2000
Xywrite

Macintosh (do not use "Fast Save")

MacWrite
Microsoft Word
WordPerfect

Other word processors should be saved as ASCII files. For files saved as ASCII, consult the editorial office regarding the keyboarding of attributes such as bold, underline, superscript, subscript, etc.

2) All design considerations for typefaces, page layout, and artwork will be handled by the publisher after receipt of the electronic manuscript. **There is no need for the author to input special typesetting codes.**

3) Be especially sure to distinguish between the letters O and I and the numbers 0 and 1, respectively.

4) A "hard return" results from tapping the keyboard's **Enter** key. Use a hard return only to end a paragraph, or for titles, subheads, separate items on a list, etc. Rely on the word processor's word wrap ("soft return") within paragraphs, list items, etc.

5) Use your word processor's capabilities for the following text attributes:

- a) bold
- b) underline and italic
- c) subscript
- d) superscript
- e) strikeout

Text that will be italic in published form may be keyboarded italic or underlined.

6) Do not use your word processor's hyphenation capabilities. Do not right justify text. Use two hyphens for long dashes.

7) In tables, use only tabs, not spaces, to align columns.

II. *Organization and Delivery of Electronic Files*

1) Accepted manuscripts may be submitted on 3.5" or 5.25" diskettes, which must be either MS-DOS or Macintosh format. The author should retain copies of all files as backup. All diskettes must be accompanied by the *final* revision and a duplicate copy of the manuscript (including two clearly separated and labeled sets of illustrations) in full conformity with the standard Information for Authors on the preceding pages.

2) Diskettes should each be labeled with:

- a) author's name
- b) short title of article
- c) operating system
- d) format
- e) word processor used, including version number.

For example, DOS/DSDD/WordPerfect 4.2, or MAC/800K/MS Word v.3. Here, *DOS* and *Mac* indicate the operating system, *DSDD* (double-sided, double density) or *800K* indicates the diskette's physical format, and the remainder indicates the word processor used. Labels for your use are available from the Editorial Office.

3) If possible, it is helpful to have additional material such as tables, figure legends, and references saved as individual files—one file for each category. A file key should accompany the diskette.

4) Submit only the final accepted version of a manuscript. It is essential that submitted electronic files exactly match the final printout.

5) Diskettes should be packed between cardboard (or with foam or bubble-wrap) in an envelope that states that magnetic media is contained.

Please submit your word-processing diskette, the final revision and a duplicate copy of your manuscript, and two clearly separated and labeled sets of illustrations to:

Thomas B. Ferguson, MD
Editor
The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041

Telephone: (314) 361-6084
FAX: (314) 367-0585

© 1992 by The Society of Thoracic Surgeons

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

■ Thirty-ninth Annual Meeting of the Southern Thoracic Surgical Association, Wesley Chapel (near Tampa), Florida—November 5–7, 1992

For information on this meeting, contact Southern Thoracic Surgical Association, 401 N Michigan Ave, Chicago, IL 60611-4267; or telephone (312) 644-6610 (facsimile: (312) 321-6869).

■ 25 Years of Myocardial Revascularization: Current Technologies and Clinical Controversies, Cleveland, Ohio—November 12–13, 1992

For information on this meeting, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 20 (facsimile: (714) 759-6911).

■ Cardiac Surgery 1993: State of the Art, St. Thomas, US Virgin Islands—November 12–14, 1992

The fifth annual conference for cardiac surgeons, perfusionists, nurses, and allied health personnel is sponsored by the Academy of Medicine of New Jersey and Cooper Hospital/University Medical Center, UMDNJ-Robert Wood Johnson Medical School at Camden. For further information, contact Rosemary Morrone: (609) 963-3757.

■ Sixty-fifth Scientific Session of the American Heart Association, New Orleans, Louisiana—November 16–19, 1992

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 373-6300 (facsimile: (214) 373-3406).

■ Le Club Mitrale, Paris, France—December 7–9, 1992

For information on this live teleconference, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870 (facsimile: (714) 759-6911).

■ Introduction to Mitral Valve Surgery, Dallas, Texas—January 21–22, 1993

For information on this live teleconference, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 20 (facsimile: (714) 759-6911).

■ First International Symposium on Thoracoscopic Surgery, San Antonio, Texas—January 22–23, 1993

For information on this meeting, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons, San Antonio, Texas—January 25–27, 1993

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

■ Third World Congress of the International Society of Cardio-Thoracic Surgeons, Salzburg, Austria—January 25–27, 1993

For information on this meeting, contact Prof Dr Felix Unger, c/o Interconvention, Austria Center Vienna, A-1450 Vienna, Austria; or telephone +43/1/23 69-26 43 (facsimile: +43/1/23 69-648).

■ Forty-second Annual Meeting of the American College of Cardiology, Anaheim, California—March 14–18, 1993

For information on this meeting, contact American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814; or telephone (800) 253-4636.

■ Le Club Mitrale, Paris, France—March 27–April 3, 1993

For information on this live teleconference, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ One Hundred Thirteenth Annual Meeting of the American Surgical Association, Baltimore, Maryland—April 1–3, 1993

For information on this meeting, contact American Surgical Association, Department of Surgery, CB 7245, University of North Carolina, 136 Burnett-Womack Building, Chapel Hill, NC 27599; or telephone (919) 966-4320 (facsimile: (919) 966-6009).

■ American College of Surgeons, Montreal, Canada—April 25–28, 1993

For information on this meeting, contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050 (facsimile: (312) 440-7014).

■ Seventy-third Annual Meeting of the American Association for Thoracic Surgery, Chicago, Illinois—April 26–28, 1993

For information on this meeting, contact American Association for Thoracic Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Fourteenth Annual Scientific Session of the North American Society of Pacing and Electrophysiology, San Diego, California—May 6–8, 1993

For information on this meeting, contact NASPE, 377 Elliot St, Newton Upper Falls, MA 02164; or telephone (617) 244-7300 (facsimile: (617) 244-3920).

■ 1993 World Symposium on Cardiomyoplasty and Biomechanical Assist, Paris, France—May 24–26, 1993

For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 22 (facsimile: (714) 759-6911).

■ The International Society for Cardiovascular Surgery/The Society for Vascular Surgery, Washington, DC—June 7–9, 1993

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ World Congress on Diseases of the Chest, Amsterdam, the Netherlands—June 13–18, 1993

For information on this meeting, contact XVII World Congress on Diseases of the Chest, International Academy of Chest Physicians & Surgeons, 3300 Dundee Rd, Northbrook, IL 60062-2348.

■ Nineteenth Annual Meeting of The Western Thoracic Surgical Association, Carlsbad, California—June 24–26, 1993

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Twenty-first World Congress of The International Society for Cardiovascular Surgery, Lisbon, Portugal—September 12–15, 1993

For information on this meeting, contact ISCVS XXIst World Congress, Congress Secretariat, 13 Elm St, Manchester, MA 01944.

■ Fifty-ninth Annual Scientific Assembly, American College of Chest Physicians, Orlando, Florida—October 24–28, 1993

For information on this meeting, contact American College of Chest Physicians, 3300 Dundee Rd, Northbrook, IL 60062; or telephone (708) 498-1400 (facsimile: (708) 498-5460).

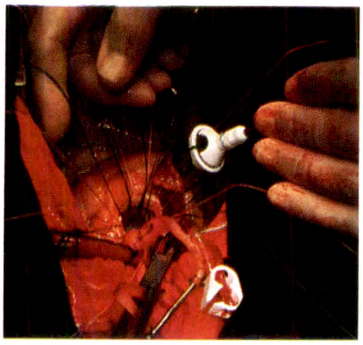
We call it Hemaflex.™ You'll call it standard operating procedure.

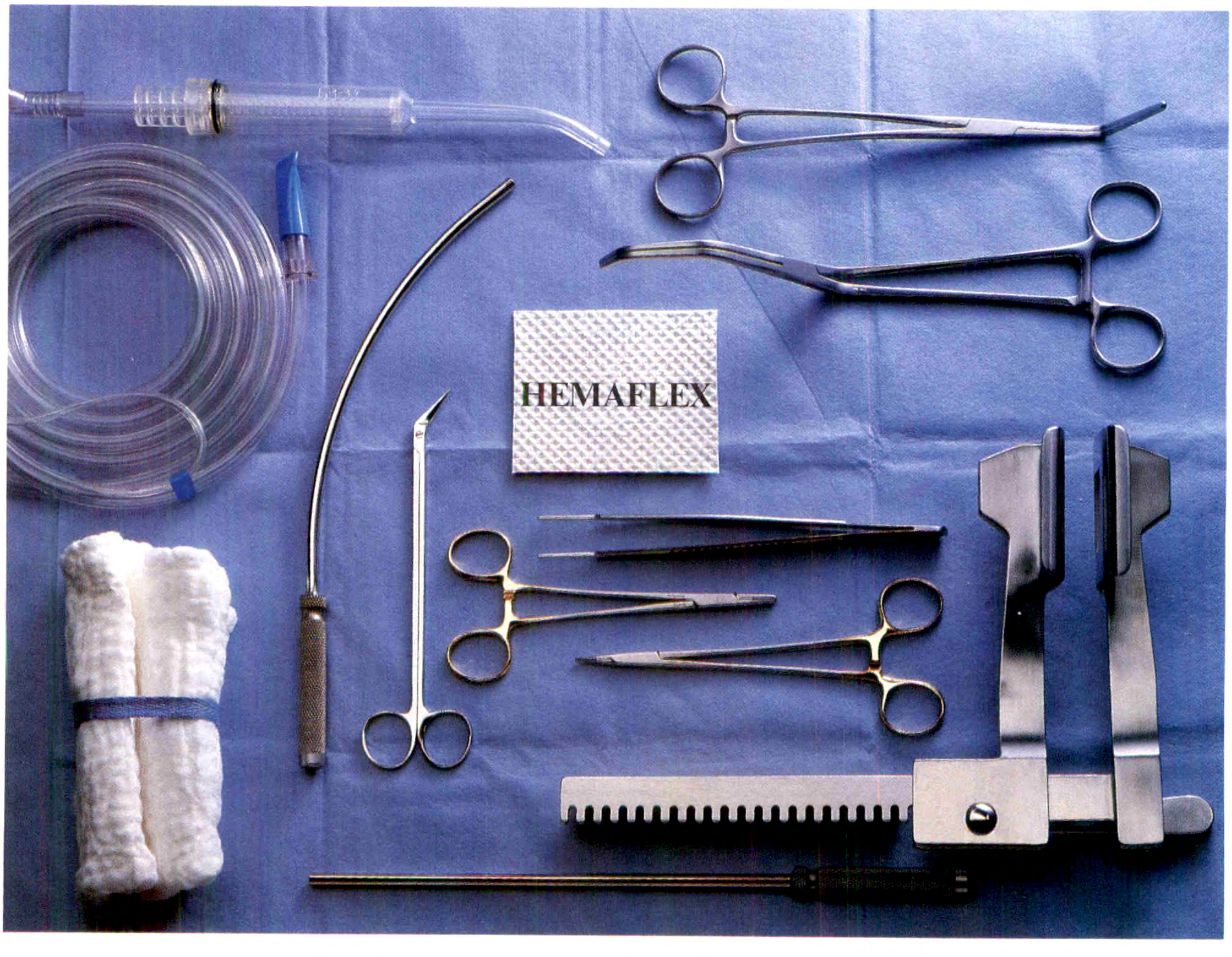
Introducing Hemaflex. It's the new, pure collagen hemostat from the makers of Avitene® (MCH). If you perform cardiovascular or cardiothoracic surgery, Hemaflex should be a part of your standard operating procedure.

- When wrapped around a vessel, Hemaflex has not been reported to have a stenotic effect, unlike other topical hemostatic agents.
- Hemaflex is effective in treating bone and soft tissue sites such as sternotomies and synthetic graft anastomoses.
- Hemaflex stops bleeding fast, unlike mechanical barriers, because it is pure collagen. It triggers the body's own blood-clotting response and is absorbed easily.
- Anticoagulation treatment does not interfere with the potent actions of Hemaflex.
- Hemaflex is easy to handle and flexible enough to wrap around vessels.

So find out for yourself why we believe Hemaflex is the ideal choice for cardiovascular and cardiothoracic procedures. Call us today at **1-800-451-4716** (in Mass., **617-938-9328**), and ask for your free sample.

HEMAFLEX™
FROM THE MAKERS OF AVITENE®





Cerebral Blood Flow and Metabolism in Hypothermic Circulatory Arrest

Craig K. Mezrow, MS, Ali M. Sadeghi, MD, Alejandro Gandsas, MD,
Howard H. Shiang, DVM, Dale Levy, MD, Robert Green, MD, Ian R. Holzman, MD,
and Randall B. Griepp, MD

Mount Sinai Medical Center, New York, New York

Although hypothermic circulatory arrest has been accepted for use in cardiovascular operations, the potential for cerebral injury exists. The mechanism of the cerebral injury remains unclear. To address these questions we studied cerebral blood flow and metabolism. Sixteen puppies were randomly assigned to undergo either 45 or 90 minutes of hypothermic circulatory arrest after perfusion/surface cooling to 13°C. Cerebral blood flow, cerebral oxygen and glucose metabolism, and cerebral vascular resistance measurements were obtained at 37°C, 13°C, 10 minutes after reperfusion, 30°C and 2 and 4 hours after hypothermic circulatory arrest. No neurologic or behavioral changes were observed in any of the long-term survivors (11/16). Metabolic and cerebral blood flow data did not differ between groups. Cerebral blood flow was significantly lower in the late postarrest measurements, whereas oxygen and glucose consumption had returned to baseline values. In the presence of low cerebral blood flow and high cerebral vascular resistance it is notable that control levels of oxygen consumption were attained by abnormally high oxygen extraction. These data strongly suggest a vulnerable interval after hypothermic circulatory arrest in which cerebral metabolism is limited by cerebral blood flow.

(Ann Thorac Surg 1992;54:609–16)

Hypothermic circulatory arrest (HCA) has facilitated the surgical repair of a wide variety of cardiovascular anomalies. The safety of HCA is largely due to a temperature-dependent reduction of metabolic rate. The brain, the organ most sensitive to ischemic injury, is the limiting factor with regard to the duration of HCA. Although clinical experience suggests that intervals of HCA of 60 minutes or shorter do not result in overt cerebral injury, the results of a number of investigations continue to raise questions about the safety of HCA duration exceeding 45 minutes. Because many of the operations requiring use of HCA in infancy frequently exceed 45 and even 60 minutes, a reexamination of the cerebral consequences of HCA seems warranted.

The present report is part of a larger study in which we are seeking to correlate intraoperative hemodynamic and metabolic variables with clinical neurological outcome after HCA. The study is being carried out in inbred weanling puppies to minimize the impact of genetic variability and to simulate as closely as possible the clinical circumstances involved in cardiac operations using HCA in infants. Our results after intervals of HCA of 45 and 90 minutes demonstrate a decrease in cerebral blood flow (CBF) and increase in cerebral vascular resistance (CVR) occurring several hours after HCA during which baseline metabolic rates are maintained only by increased extraction of oxygen and glucose. We believe that this constitutes a period of increased vulnerability to cerebral injury after HCA.

Material and Methods

Sixteen weanling beagles (Marshall Farms, North Rose, NY), 3 to 4 months of age, weighing 6 to 7 kg, were randomly assigned to one of two experimental groups, either to undergo 45 or 90 minutes of HCA. Each experimental group underwent preoperative neurologic and behavioral assessment, invasive intraoperative measurements, and a postoperative neurologic and behavioral evaluation.

Anesthesia

Animals were pretreated with glycopyrrolate (0.025 mg/kg), anesthetized with fentanyl (25 to 50 $\mu g \cdot kg^{-1} \cdot h^{-1}$) and isoflurane (<1%), and intubated. They were maintained on positive-pressure ventilation (inspired oxygen fraction >0.40; carbon dioxide tension, 35 to 40 mm Hg) and paralyzed with pancuronium. This regimen, in which blood gases were monitored according to so-called alphastat principles, is similar to that used clinically in infants, and was selected to maintain conditions that would seek to minimize changes in CBF and oxygen and glucose metabolism. Arterial oxygen tension was maintained greater than 100 mm Hg. Lead II was used for electrocardiographic monitoring. Temperature probes were placed in the esophagus and rectum, and an indwelling catheter was inserted in the bladder. Femoral artery and vein cannulations were performed for monitoring purposes.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Mezrow, Department of Cardiothoracic Surgery, Mount Sinai Medical Center, PO Box 1028, New York, NY 10029.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

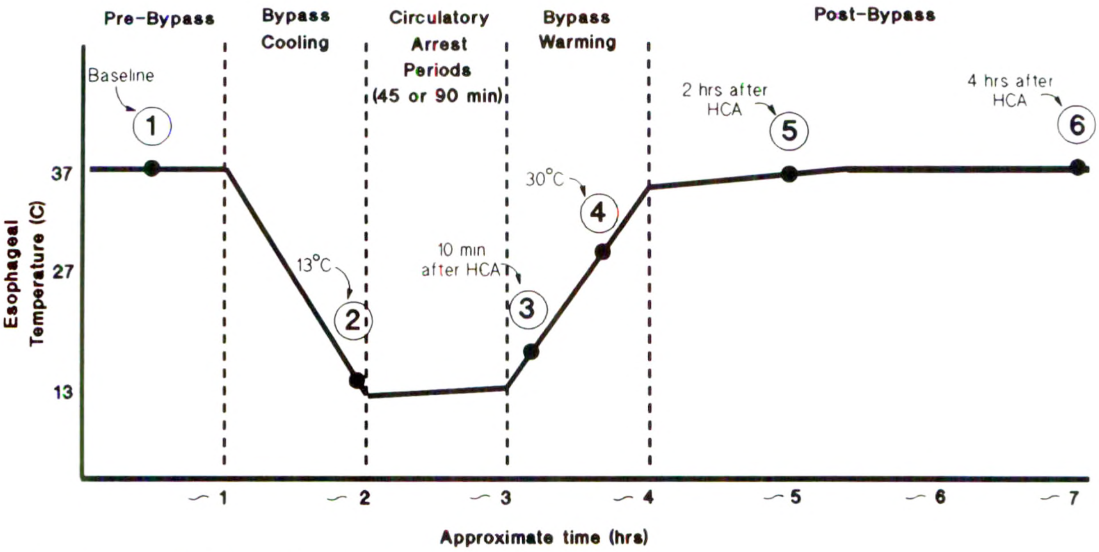


Fig 1. Measurement time points. (HCA = hypothermic circulatory arrest.)

Sagittal Sinus Cannulation

Sagittal sinus cannulation was performed before cannulation for cardiopulmonary bypass (CPB). A midline scalp incision was made and the underlying periosteum removed to facilitate identification of the coronal and sagittal sutures. Under 2.5× magnification, a 3-mm cutting burr was used to remove the bone over the sinus. A 24-gauge catheter was inserted into the sagittal sinus to permit both sampling of cerebral venous blood and monitoring of cerebral venous pressure.

Cardiopulmonary Bypass, Cooling, and Rewarming

After heparinization (300 IU/kg), nonpulsatile CPB was instituted employing single-cannula drainage of the right atrium with return of the arterial perfusate through a cannula positioned in the ascending aorta. A cannula was passed from the left atrium into the left ventricle to permit decompression of the left heart during CPB. Surface cooling was achieved using both a cooling blanket and ice packs around the head. Membrane oxygenators (VPCML plus; Cobe Laboratories, Inc, Lakewood, CO) were primed with a hemodilute solution containing homologous blood (universal donor), 5% albumin solution, furosemide (1 mg/kg), heparin (2,000 IU), 1% dextrose in 0.9% saline solution, and KCl (1 mEq/kg). Cardiopulmonary bypass was established at 75 to 100 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and hematocrit was maintained between 0.22 and 0.28. Employing the principles of alpha-stat management, pH during cooling was maintained at 7.4 ± 0.05 and carbon dioxide tension at 35 to 40 mm Hg, uncorrected for temperature. Cooling was carried out to an esophageal temperature of 13°C. The total period of perfusion cooling varied from 50 to 60 minutes. Circulatory arrest was then established and the perfusate drained into the oxygenator reservoir. After the selected interval of HCA (45 or 90 minutes), perfusion/surface rewarming was carried out (CPB at 75 to 100 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for 50 to 60 minutes) to an esophageal temperature of more than 36°C and the animals then weaned from CPB. When necessary, cardiac defibrillation was performed after administration of lidocaine (1 mg/kg). After decannulation, protamine sulfate (5 mg/kg) was administered to reverse heparinization.

Table 1. Comparison of Perfusion Cooling and Rewarming Time[a]

Group	Weight (kg)	CPB Cooling (min)	CPB Warming (min)
45 min HCA (n = 8)	6.8 ± 0.5	53 ± 2	52 ± 3
90 min HCA (n = 8)	7.0 ± 0.4	56 ± 2	53 ± 2

[a] Values are shown as mean ± standard error.

CPB = cardiopulmonary bypass; HCA = hypothermic circulatory arrest.

Cerebral Blood Flow and Cerebrovascular Resistance

Cerebral blood flow was measured using radionuclide-labeled microspheres as originally described by Rudolph and Heymann [1]. Approximately 0.5 to 1.5 × 10^6 microspheres 15 ± 0.5 μm in diameter labeled with Ru^{103}, Sn^{113}, Cr^{51}, Co^{57}, Nb^{95}, and Sc^{46} (New England Nuclear, Wilmington, DE) were injected and flushed with 5 mL of saline solution into a transthoracic left ventricular catheter before and after CPB, and into the arterial cannula during CPB. Blood reference samples were withdrawn from the femoral arterial line at a constant rate (2.29 mL/min) with a Harvard withdrawal pump beginning 15 seconds before microsphere injection and ending 105 seconds after injection.

After postoperative neurologic and behavioral evaluation (details described later), the animals were anesthetized and sacrificed using sodium pentobarbital (30 mg/kg) and KCl (6 mEq/kg). In all animals (including those who succumbed), each brain was removed and weighed, and radionuclide determination was made using a gamma counter (Auto-Gamma, Packard Instruments). Analyses were carried out by computer solution of multiple simultaneous linear equations (Compusphere; Packard Instruments, Downer's Grove, IL). Cerebral blood flow was calculated using the following equation:

Table 2. Acid-Base, Blood Gas, and Hemodynamic Variables[a]

Variable	Baseline (37°C)	13°C	10 min After HCA	30°C	2 h After HCA	4 h After HCA
Esophageal Temperature (°C)						
45 min HCA	36.5 ± 0.3	12.8 ± 0.1	16.2 ± 0.5	30.7 ± 0.6	35.5 ± 0.4	37.2 ± 0.9
90 min HCA	36.4 ± 0.3	12.6 ± 0.1	17.1 ± 0.5	29.8 ± 0.2	35.3 ± 0.5	36.8 ± 0.1
MAP (mm Hg)						
45 min HCA	88 ± 8	52 ± 5	55 ± 4	57 ± 4	81 ± 5	93 ± 5
90 min HCA	87 ± 5	53 ± 4	63 ± 4	46 ± 6	83 ± 2	97 ± 2
pHa						
45 min HCA	7.35 ± 0.02	7.37 ± 0.01	7.38 ± 0.02	7.35 ± 0.01	7.37 ± 0.02	7.39 ± 0.02
90 min HCA	7.33 ± 0.01	7.37 ± 0.02	7.37 ± 0.02	7.31 ± 0.14	7.38 ± 0.11	7.37 ± 0.01
PaO_2 (mm Hg)						
45 min HCA	594 ± 20	453 ± 61	486 ± 48	286 ± 55	579 ± 62	633 ± 16
90 min HCA	615 ± 12	437 ± 26	623 ± 54	407 ± 31	638 ± 16	634 ± 13
$PaCO_2$ (mm Hg)						
45 min HCA	38 ± 1	35 ± 2	36 ± 1	33 ± 1	36 ± 2	37 ± 1
90 min HCA	39 ± 1	34 ± 1	32 ± 2	32 ± 2	35 ± 1	39 ± 1
Hematocrit						
45 min HCA	0.36 ± 0.01	0.27 ± 0.01	0.23 ± 0.01	0.24 ± 0.01	0.33 ± 0.02	0.35 ± 0.02
90 min HCA	0.36 ± 0.01	0.25 ± 0.01	0.21 ± 0.01	0.23 ± 0.01	0.30 ± 0.02	0.33 ± 0.02

[a] Values are shown as mean ± standard error.

HCA = hypothermic circulatory arrest; MAP = mean arterial pressure; $PaCO_2$ = carbon dioxide tension; PaO_2 = oxygen tension.

$$\text{CBF}\ (\text{mL}\cdot 100\ \text{g}^{-1}\cdot \text{min}^{-1}) = (\text{cerebral tissue counts} \times \text{rate of withdrawal}) \times 100/(\text{counts in reference sample} \times \text{brain weight}).$$

Cerebral vascular resistance was calculated by using the equation:

$$\text{CVR}\ (\text{mm Hg}\cdot \text{mL}^{-1}\cdot 100\ \text{g}^{-1}\cdot \text{min}^{-1}) = (\text{MAP} - \text{MSSP})/\text{CBF},$$

where MAP = mean arterial pressure and MSSP = mean sagittal sinus pressure.

Cerebral Metabolism

Sagittal sinus and arterial samples were obtained simultaneously for calculation of both cerebral oxygen extraction (arteriovenous oxygen content difference) and glucose extraction (arteriovenous glucose difference). Cerebral metabolic rate of oxygen ($CMRO_2$) and cerebral metabolic rate of glucose (CMRGlu) were determined as follows:

$$CMRO_2\ (\text{mL}\cdot 100\ \text{g}^{-1}\cdot \text{min}^{-1}) = \text{CBF} \times (\text{arterial } O_2 \text{ content} - \text{sagittal sinus } O_2 \text{ content})/100.$$

$$\text{CMRGlu}\ (\text{mg}\cdot 100\ \text{g}^{-1}\cdot \text{min}^{-1}) = \text{CBF} \times (\text{arterial glucose} - \text{sagittal sinus glucose})/100.$$

Arterial and venous blood pH, oxygen tension, carbon dioxide tension, hematocrit, and oxygen content were measured using a Ciba-Corning Diagnostics Corporation analyzer (model 288; Medfield, MA), and glucose levels were determined using a YSI Inc analyzer (model 2300; Yellow Springs, OH).

Study Protocol

Measurements of CBF, CVR, $CMRO_2$, and CMRGlu were made at six time points during the experiments (Fig 1): (1)

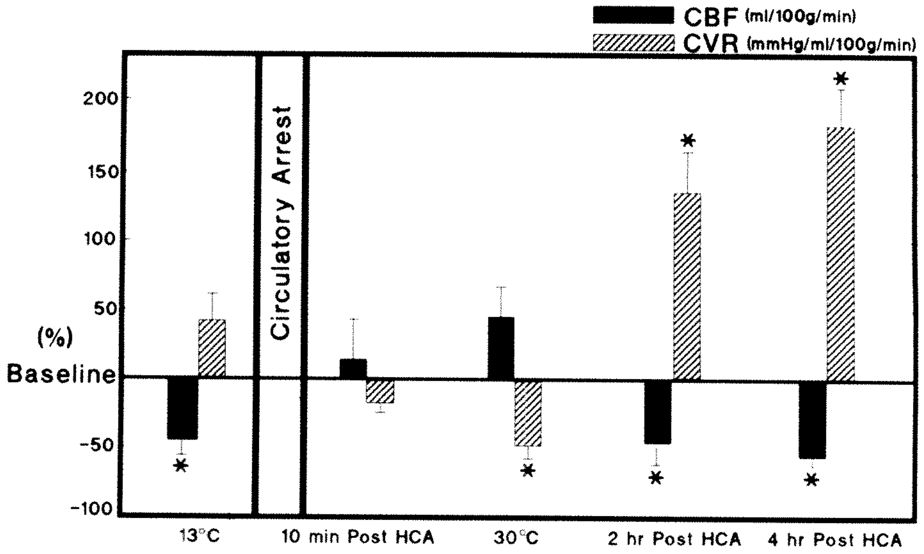
Table 3. Cerebral Blood Flow and Vascular Resistance[a]

			Perfusion Rewarming			
Variable	Baseline (37°C)	13°C	10 min After HCA	30°C	2 h After HCA	4 h After HCA
CBF (mL · 100 g^{-1} · min^{-1})						
45 min HCA	90 ± 18	41 ± 9[b]	65 ± 11	93 ± 10	31 ± 3[b]	40 ± 10[b]
90 min HCA	74 ± 9	36 ± 7[b]	87 ± 30	106 ± 18	41 ± 9[b]	30 ± 2[b]
CVR (mm Hg · mL^{-1} · 100 g^{-1} · min^{-1})						
45 min HCA	1.0 ± 0.1	1.3 ± 0.1	0.8 ± 0.1	0.6 ± 0.1[b]	2.6 ± 0.3[b]	2.7 ± 0.3[b]
90 min HCA	1.2 ± 0.2	1.6 ± 0.2	0.9 ± 0.1	0.5 ± 0.1[b]	2.0 ± 0.4[b]	3.1 ± 0.3[b]

[a] Values are shown as mean ± standard error. [b] $p < 0.05$ versus baseline (37°C).

CBF = cerebral blood flow; CVR = cerebral vascular resistance; HCA = hypothermic circulatory arrest.

*Fig 2. Cerebral blood flow (CBF) and vascular resistance (CVR) (mean values ± standard error). (HCA = hypothermic circulatory arrest; *p < 0.05 versus baseline by analysis of variance.)*



baseline: at 37°C before CPB; (2) after cooling, immediately before HCA at 13°C; (3) 10 minutes after the end of HCA; (4) during rewarming at 30°C (approximately 20 minutes after the end of HCA); (5) 2 hours after the end of HCA (after termination of CPB, at 37°C with closed thorax); and (6) 4 hours after the end of HCA.

Behavioral and Neurological Assessment

Puppies were examined preoperatively and observed for 1 week postoperatively for evaluation of behavioral and neurological sequelae of HCA. They were evaluated daily by a veterinarian unaware of the experimental design to determine whether behavioral changes were present (mental status, appetite, affect). Each animal also underwent neurological examination including evaluation of gait, reflexes, and cranial nerve responses.

Statistical Analysis

All results are expressed as the mean ± standard error. A *p* value less than 0.05 as determined by analysis of variance was accepted as statistically significant.

Perioperative Management

All animals have received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). The protocol for these experiments was approved by the Mount Sinai Institutional Animal Care Committee, and the animals were housed in the institution's NIH-approved animal facility preoperatively and postoperatively.

Results

Demographic data are displayed in Table 1. There was no difference between the groups of puppies undergoing 45 or 90 minutes of HCA with respect to weight or duration of CPB.

Table 2 shows the controllable variables measured for each animal at the six times that data were collected for calculation of CBF and cerebral metabolism in each group. As intended by the design of the study, there were no significant differences between animals in the two groups in terms of temperature, mean arterial pressure, arterial pH, blood gases, or hematocrit at any of the time points.

Long-Term Survival/Neurological Evaluation

Although all animals included in the study survived long enough to complete the intraoperative protocol and were successfully weaned from CPB, 7 of 8 animals survived for 1 week after 45 minutes of HCA, but only 4 of 8 survived after 90 minutes of HCA. All deaths were attributed to noncardiogenic pulmonary congestion. No neurologic or behavioral changes were present in any of the surviving animals.

Cerebral Blood Flow and Cerebral Vascular Resistance

The values for CBF and CVR for the six time points for animals undergoing 45 minutes and those undergoing 90 minutes of HCA are shown in Table 3. There being no differences between the two groups, the data for both groups were combined in Figures 2 and 3A.

There was a significant decrease in CBF at 13°C before HCA compared with baseline values before CPB at 37°C. During rewarming, CBF very rapidly returned to baseline values, but then fell markedly by 2 hours after the end of HCA and remained significantly lower than baseline values 4 hours after HCA (see Fig 2).

Cerebral vascular resistance did not show a significant increase upon cooling but decreased during rewarming: a difference from baseline was significant at the 30°C timepoint (Fig 3B; see Table 3). By 2 hours after HCA, however, CVR was markedly increased, and it remained significantly higher than baseline 4 hours after HCA.

Cerebral Oxygen Metabolism

There were no significant differences between groups with different durations of HCA with regard to sagittal sinus oxygen saturation, oxygen extraction, or $CMRO_2$ (Table 4). Hence, the values for both groups were combined in Figures 3C, 3D, and 4.

As might have been predicted, oxygen extraction and

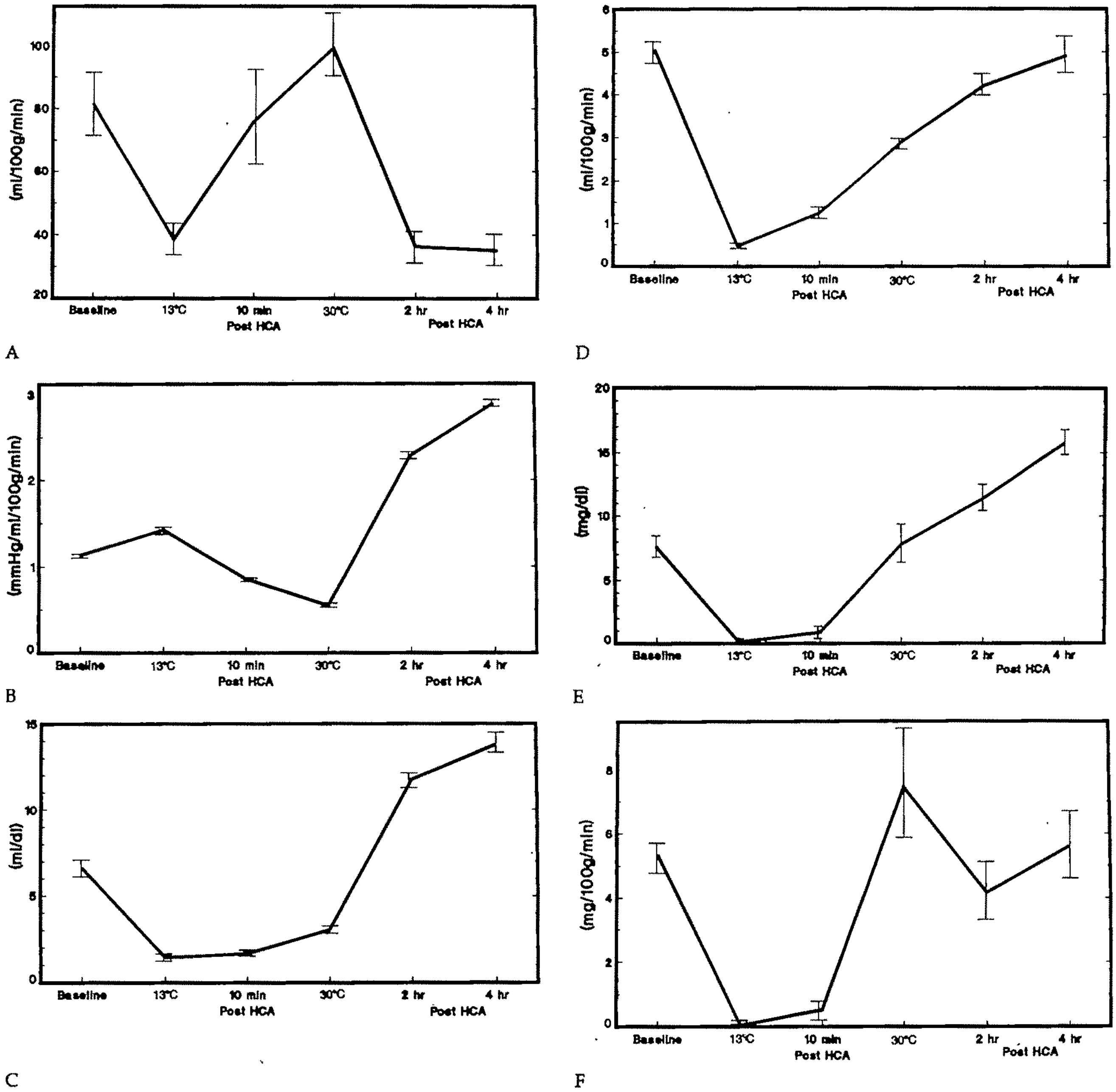


Fig 3. (A) Cerebral blood flow. (B) Cerebral vascular resistance. (C) Oxygen extraction. (D) Cerebral metabolic rate of oxygen. (E) Glucose extraction. (F) Cerebral metabolic rate of glucose. All values are shown as mean ± standard error. (HCA = *hypothermic circulatory arrest.)*

consumption were markedly reduced by cooling and remained lower than baseline values as rewarming began. By 2 hours after HCA, however, at a time when oxygen consumption had returned to levels not significantly different from baseline values, oxygen extraction had risen to levels significantly higher than control values, correlating with significantly depressed sagittal sinus oxygen saturations.

Cerebral Glucose Metabolism

No notable differences between the experimental groups were present with regard to glucose extraction and CMRGlu (Table 5). As was seen with oxygen consumption, glucose extraction was markedly reduced during cooling and early rewarming (see Fig 3E). As was the case with oxygen metabolism, by 2 hours after HCA CMRGlu had returned to levels not significantly different from baseline values but glucose extraction had risen to levels significantly higher than baseline values; the levels of glucose extraction remained significantly elevated 4 hours after HCA (see Figs 3E, 3F).

Summary of Results

The relationship between the changes in CBF, CVR, and cerebral metabolism can perhaps best be summarized by taking the ratio CBF/CMRO$_2$ (Fig 5). If the baseline value of this ratio is assumed to represent normal cerebral autoregulation, ie, an optimal relationship between CBF

Table 4. Cerebral Oxygen Saturation and Metabolism[a]

	Baseline (37°C)	13°C	10 min After HCA	30°C	2 h After HCA	4 h After HCA
SS O_2 sat (%)						
45 min HCA	67 ± 5	95 ± 2[b]	94 ± 2[b]	78 ± 3	29 ± 3[b]	24 ± 1[b]
90 min HCA	73 ± 3	96 ± 1[b]	97 ± 1[b]	79 ± 3	33 ± 2[b]	25 ± 2[b]
O_2 extraction (mL/dL)						
45 min HCA	6.9 ± 0.8	1.5 ± 0.3[b]	1.6 ± 0.2[b]	2.9 ± 0.3[b]	12.4 ± 0.5[b]	14.1 ± 0.7
90 min HCA	6.4 ± 0.6	1.3 ± 0.3[b]	1.7 ± 0.2[b]	3.1 ± 0.3[b]	11.1 ± 0.5[b]	13.4 ± 0.8
$CMRO_2$ ($mL \cdot 100\ g^{-1} \cdot min^{-1}$)						
45 min HCA	5.6 ± 1.2	0.5 ± 0.1[b]	1.0 ± 0.1[b]	2.7 ± 0.4	3.8 ± 0.3	5.8 ± 2.1
90 min HCA	4.5 ± 0.6	0.4 ± 0.1[b]	1.5 ± 0.8[b]	3.1 ± 0.5	4.6 ± 1.3	4.0 ± 0.4

[a] Values are shown as mean ± standard error. [b] $p < 0.05$ versus baseline (37°C).

$CMRO_2$ = cerebral metabolic rate of oxygen; HCA = hypothermic circulatory arrest; O_2 extraction = arteriovenous oxygen content difference; SS O_2 sat = sagittal sinus oxygen saturation.

and cerebral metabolism, then CBF is excessive—this has been dubbed "luxury perfusion" during cooling and immediately upon rewarming. Late after HCA, the ratio $CBF/CMRO_2$ falls well below its optimal value so that normal or slightly increased rates of cerebral metabolism can only be maintained by means of increased extraction of oxygen and glucose. The inappropriately high CBF during cooling is reflected by—or perhaps a consequence of—the unchanged CVR during cooling, and the decrease in CBF at the late time points is correlated with a marked increase in CVR.

Comment

Although there is some uncertainty concerning the safe duration of HCA, there is almost universal agreement that when the duration of HCA exceeds 60 minutes there is increased risk of cerebral injury. It is not known whether the cerebral injury that can occur as a consequence of HCA takes place during the period of circulatory arrest or during reperfusion. The mechanism of injury also remains unknown. To address these questions we investigated the impact of "safe" (45 minutes) and potentially "unsafe" (90 minutes) intervals of HCA on CBF, CVR, $CMRO_2$, and CMRGlu. We also sought to correlate these intraoperative variables with neurological outcome.

We were surprised by the fact that there was no evidence of adverse neurological outcome in any of the animals surviving 90 minutes of HCA. The animals who died did not live long enough to ascertain whether they had any overt neurological deficits. Moreover, there were no significant differences in measured variables between those puppies who survived and those who died after operation in both HCA groups. All deaths occurred within 24 hours of CPB and were attributed to noncardiogenic pulmonary congestion, a complication of our CPB technique.

Given the absence of any significant differences between the two groups either in neurological or behavioral outcome or in intraoperative measures of cerebral blood flow or metabolism, we suggest that no obvious cerebral injury is discernible under conditions of 90 minutes of HCA at 13°C employing combined surface and perfusion cooling and rewarming. We recognize that clinical studies that have shown effects of longer intervals of HCA have generally shown subtle impairment of cognitive function, and that without the ability to measure intelligence in our animal model, we would need sophisticated quantitative electroencephalographic analysis and careful postmortem histological evaluation of the brain before firmly concluding that no cerebral damage has occurred even after the longer intervals of HCA used in this study. Although histopathological assessment of these animals is not complete, past experience with this model suggests that when no clinical evidence of cerebral injury is present unequivocal histopathological changes are unlikely to be found.

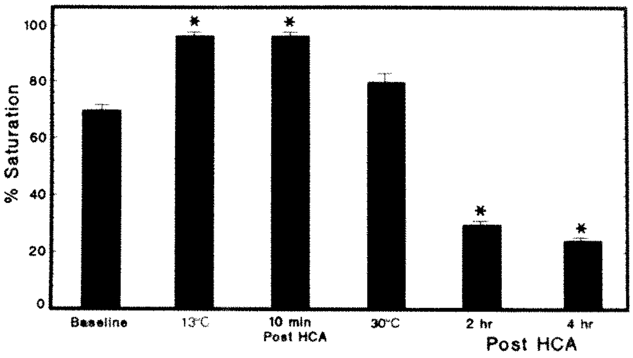


*Fig 4. Cerebral venous oxygen saturation (mean values ± standard error). (HCA = hypothermic circulatory arrest; *p < 0.05 versus baseline by analysis of variance.)*

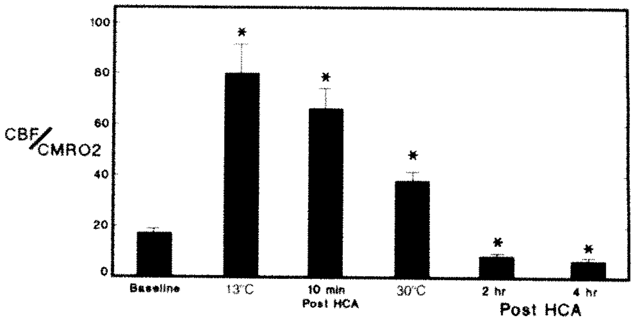


*Fig 5. Relationship of cerebral blood flow (CBF) to cerebral metabolic rate of oxygen (CMRO2) (mean values ± standard error). (HCA = hypothermic circulatory arrest; *p < 0.05 versus baseline by analysis of variance.)*

Table 5. Cerebral Glucose Metabolism[a]

Variable	Baseline (37°C)	13°C	10 min After HCA	30°C	2 h After HCA	4 h After HCA
Glucose extraction (mg/dL)						
45 min HCA	7 ± 1	0.3 ± 0.2[b]	1 ± 0.4[b]	6 ± 2	12 ± 2[b]	15 ± 1[b]
90 min HCA	8 ± 1	0 ± 0[b]	1 ± 1[b]	10 ± 3	11 ± 1	17 ± 2[b]
CMRGlu ($mg \cdot 100\ g^{-1} \cdot min^{-1}$)						
45 min HCA	5.1 ± 0.4	0.1 ± 0.1[b]	0.3 ± 0.2[b]	6.0 ± 2.3	3.4 ± 0.5	6.2 ± 2.0
90 min HCA	5.6 ± 0.8	0 ± 0[b]	0.7 ± 0.5[b]	8.9 ± 2.6	4.9 ± 1.6	5.0 ± 0.6

[a] Values are shown as mean ± standard error. [b] $p < 0.05$ versus baseline (37°C).

CMRGlu = cerebral metabolic rate of glucose; glucose extraction = arteriovenous glucose difference; HCA = hypothermic circulatory arrest.

The decrease in CBF and cerebral metabolism during cooling is in accord with theoretical predictions and the experimental work of others [2, 3]. The marked reduction in oxygen and glucose metabolism just before HCA at 13°C add to available evidence demonstrating the theoretical safety of circulatory arrest at this temperature. The earliest measurements of oxygen and glucose metabolism after the interval of HCA are also reassuringly low, suggesting that cerebral metabolism is relatively quiescent during even the longer interval of circulatory arrest.

During rewarming (30°C), both oxygen and glucose metabolism returned to near baseline values but oxygen extraction remained depressed. This may reflect a persistent effect of low temperature on glucose and oxygen extraction or the fact the CBF is actually excessive relative to both temperature and metabolic requirements so that less extraction is required to meet metabolic demands.

The increase in CVR and decrease in CBF after HCA are in agreement with the work of others using a variety of methods for the study of CBF [2–5]. The contribution that our study makes is in showing that this decreased CBF appears to be inappropriate in terms of the metabolic demands of the brain during its recovery from HCA. The discordance between CBF and cerebral metabolism suggests that there is a disturbance in cerebral autoregulation after HCA, and by monitoring these variables longer after HCA than has been done previously, we have shown that the inappropriately depressed CBF and increased CVR last at least 4 hours. We cannot be sure from our data whether even higher metabolic rates would not be better for optimal cerebral recovery, or whether at some point beyond 4 hours after HCA the decrease in CBF becomes so severe that a further increase in oxygen extraction cannot take place to maintain the appropriate metabolic rate.

In this study, the decrease in CBF observed in the late postoperative period was unrelated to any change in mean arterial pressure or other adverse postoperative event and was apparently adequately compensated for by increased extraction of both oxygen and glucose to maintain the cerebral metabolic rate at baseline levels. It seems likely, however, that any decrease in arterial pressure, decreased hematocrit, or hypoxia might impair oxygen delivery during this interval of reduced CBF. We are persuaded that this late reperfusion period is a time when the brain is particularly vulnerable to injury because even under optimal circumstances it is already relying on reserve mechanisms to maintain cerebral metabolism.

Our study suggests that an interval of impaired CBF occurs even after "safe" intervals of HCA. Further studies will be needed to define the length of the vulnerable interval after HCA and to determine whether this period of increased potential for cerebral injury is also present after clinical alternatives to HCA such as low-flow moderately hypothermic perfusion.

Supported by grant HL-45636-02 from the National Heart, Lung, and Blood Institute.

We thank Rashin Nouranifar and Luigi Compere for their technical assistance in the conduct of these experiments.

References

1. Rudolph AM, Heymann MA. The circulation of the fetus in utero: methods for studying distribution of blood flow, cardiac output and organ blood flow. Circ Res 1967;21:163–84.
2. Greeley WJ, Kern FH, Ungerleider RM, et al. The effect of hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral metabolism in neonates, infants, and children. J Thorac Cardiovasc Surg 1991;101:783–94.
3. Perna AM, Gardner TJ, Tabaddor K, Brawley RK, Gott VL. Cerebral metabolism and blood flow after circulatory arrest during deep hypothermia. Ann Surg 1973;178:95–101.
4. Settergren G, Öhqvist G, Lundberg S, Henze A, Björk VO, Persson B. Cerebral blood flow and cerebral metabolism in children following cardiac surgery with deep hypothermia and circulatory arrest. Clinical course and follow-up of psychomotor development. Scand J Thorac Cardiovasc Surg 1982; 16:209–15.
5. Hillier SC, Burrows FA, Bissonnette B, Taylor RH. Cerebral hemodynamics in neonates and infants undergoing cardiopulmonary bypass and profound hypothermic circulatory arrest: Assessment by transcranial Doppler sonography. Anesth Analg 1991;72:723–8.

DISCUSSION

DR RICHARD A. JONAS (Boston, MA): I want to congratulate you on an excellent presentation of a very interesting study. In Boston we have also developed a model of circulatory arrest in neonatal piglets and have been looking at similar parameters. We concur with your finding that cerebral metabolic rate determined by oxygen extraction has returned to baseline within about 3 hours after 60 minutes of circulatory arrest at a nasopharyngeal temperature of 15°C.

I have two questions. You said in your conclusion that you believed there was a potentially vulnerable period where decreased pressure might result in inadequate cerebral perfusion. This is equivalent to a loss of cerebral autoregulation, in other words, pressure passive cerebral blood flow. Is that in fact what you found? You stated that you found that there was some uncoupling of cerebral metabolic rate and cerebral blood flow, but that is not the same as loss of pressure/flow autoregulation.

MR MEZROW: Our findings after cardiopulmonary bypass revealed that there is an interval of cerebral hypoperfusion in which cerebral metabolism is maintained by abnormally high oxygen extraction. We refer to this period as "the vulnerable period" because if there were to be any further decrease in cerebral perfusion or oxygen carrying capacity, further increases in cerebral oxygen extraction to maintain cerebral metabolism may not be possible and cerebral injury may ensue.

DR JONAS: Did you specifically look at cerebral blood flow versus systemic blood pressure?

MR MEZROW: It was not the intent of this study to investigate the relationship of arterial blood pressure to cerebral blood flow. All measurements in this study were performed with similar mean arterial pressures and hematocrit values.

DR JONAS: But these animals were off bypass.

MR MEZROW: All postbypass measurements were performed with mean arterial pressures similar to baseline values.

DR JONAS: My second question relates to pH strategy. In 1985 we changed clinically from pH-stat to alpha-stat strategy. We subsequently noted several cases of choreoathetosis after deep hypothermic circulatory arrest for complex anomalies. A recent retrospective neurodevelopmental study at Children's Hospital has indicated that the use of alpha-stat with circulatory arrest has been associated with a worse cognitive outcome relative to the more acidotic strategy that we were using previously. Have you any information regarding the influence of pH strategy in your study?

MR MEZROW: We employed alpha-stat blood gas management during the conduct of this study as it is performed clinically at our institution. This study was designed to mimic the clinical practices at our institution as closely as possible. We have no data to suggest alpha-stat blood gas management to be superior to pH-stat blood gas management, but we believe there are numerous studies to suggest this.

DR ROSS M. UNGERLEIDER (Durham, NC): I would like to congratulate you on this study, and especially for focusing attention on this area that is important for neonatal heart surgeons. I also congratulate you for performing behavioral studies in puppies. I think that is remarkable!

I do have a couple of questions about your model. Number one, you do not really have any control animals, that is, animals that were subjected to cardiopulmonary bypass and hypothermia without total circulatory arrest and rewarmed, and it leads me to question whether the changes we are seeing are entirely due to circulatory arrest or to the model itself. Do you have those data?

Second, I am interested in your initial statement that you chose two periods of circulatory arrest, 45 minutes being so-called "safe" and 90 minutes being "unsafe," and yet you did not see any differences between these groups. Are we supposed to assume then that there is no difference between the "safe" versus "unsafe" times? By combining these data, have you obscured valuable information? More importantly, from our own studies, I am surprised you found no difference.

Finally, I just have a question regarding the cerebral blood flow and metabolic changes. In babies we have found that there is a deficit in $CMRO_2$ immediately after hypothermic circulatory arrest. It does recover after a period of time. I wonder if the fact that you waited 2 hours until you obtained your first data point may mean that you might have missed depressed cerebral metabolism had you obtained data sooner. In fact, when I look at the decreased cerebral blood flow I wonder immediately, are your cardiac output and hemodynamics identical to the prearrest time or is blood flow diminished to the entire animal, or if cerebral blood flow was diminished, where is the increased flow going?

But overall I would like to congratulate you on an interesting study.

MR MEZROW: With regard to your question of controls, we did not perform a control group of animals not undergoing periods of circulatory arrest. This study was designed for every animal to be its own control with baseline measurements. We are currently investigating cerebral blood flow and metabolism after periods of hypothermic low-flow cardiopulmonary bypass.

With regard to your question of the "safe" and "unsafe" periods of hypothermic circulatory arrest investigated, we were surprised by the fact that there was no evidence of adverse neurological outcome in any of the animals surviving 90 minutes of hypothermic circulatory arrest. There were no significant differences in measured variables between those animals subjected to 45 or 90 minutes of hypothermic circulatory arrest. Without the sophisticated measurements of quantitative electroencephalography and histopathologic evaluations of the brain we cannot conclude with any certainty that there was absence of cerebral injury in animals subjected to 90 minutes of hypothermic circulatory arrest.

With regard to your question of $CMRO_2$ immediately after hypothermic circulatory arrest, our measurement time points after circulatory arrest were 10 minutes after circulatory arrest, 30°C esophageal temperature, and 2 and 4 hours after circulatory arrest. Approximately 1 hour separates the 30°C and 2 hour postarrest measurements. Our 30°C data of decreased $CMRO_2$ concur with those you describe in your babies immediately after circulatory arrest. We believe this is due to the hypothermic state of the patient.

With regard to your question of cardiac output and hemodynamics after circulatory arrest compared with before cardiopulmonary bypass, all measurements were made with similar hemodynamic variables such as mean arterial pressure and hematocrit values. We performed cardiac output measurements in several animals in this study and found no significant differences in prebypass and postbypass measurements, suggesting that postbypass cerebral hypoperfusion is not due to altered cardiac function.

Does a Posterior Aneurysm Increase the Risk of Endocardial Resection?

Irving L. Kron, MD, John A. Kern, MD, Pierre Theodore, BA, Terry L. Flanagan, MPH, David E. Haines, MD, Michael J. Barber, MD, and John P. DiMarco, MD, PhD

Division of Thoracic and Cardiovascular Surgery and Division of Cardiology, University of Virginia Health Sciences Center, Charlottesville, Virginia

The bias has been that the ideal anatomic circumstance for endocardial resection is the anterior left ventricular location. Posterior left ventricular aneurysms have been thought to be problematic to map and more difficult to close, and possibly to have a different substrate for ventricular tachycardia. To address this problem, we retrospectively reviewed the cases of 110 consecutive patients who underwent sequential endocardial resection for ventricular tachycardia between 1983 and 1991. Ninety-six patients had an anterior aneurysm, and 14 patients had a posterior aneurysm or infarct. Operative survival and 5-year survival were very similar between the two groups (p = not significant). A positive postoperative electrophysiological study was present in 11% of the anterior group versus 14% of the posterior group (p = not significant). There was a significantly greater incidence of mitral valve replacement in the posterior group, and we believe this was most likely due to frequent localization of the arrhythmia to the papillary muscle. Otherwise, patients with a posterior aneurysm or infarct had surgical results equivalent to those in patients with an anterior location. As long as there is a discrete aneurysm or infarct, endocardial resection is a safe and effective therapeutic procedure for ventricular tachycardia.

(Ann Thorac Surg 1992;54:617–20)

Since the development of endocardial resection for the surgical treatment of ventricular tachyarrhythmias (VTs), the posterior location of a scar or aneurysm has resulted in poorer surgical results than the anterior location. Two of the three early failures because of incomplete resection in the initial description of this operation by Horowitz and associates [1] were related to the posterior papillary muscle being the site of origin of the arrhythmia. Hammon and colleagues [2] suggested that the anterior location of VTs usually provides a good result with a predicted mortality rate of 5% or less versus the inferior origin, which has a higher incidence of persistent arrhythmias postoperatively. Miller and co-workers [3] confirmed this observation and noted that an inferior site of tachycardia is not as ideal in this situation as an anterior location. We [4] also believe this. As a result, we [5] have preferred to treat the inferiorly located aneurysm medically or with an automatic implantable cardioverter defibrillator, as the results after resection have not been as predictable. Therefore, we decided to review retrospectively our experience with ventricular tachycardia resulting from inferior-posterior infarction to see if our initial bias was correct.

Material and Methods

Patient Characteristics

There were 110 patients who underwent sequential endocardial resection for VT between July 1983 and December 1991 at the University of Virginia Health Sciences Center. In 96, the aneurysm was located anteriorly, and in 14, the aneurysm or infarct had a posterior location. Specific patient characteristics are listed in Table 1.

Preoperative Evaluation

The workup was similar for both patient groups. All patients had clinically documented sustained VT or a history of cardiac arrest. After cardiac catheterization, each patient underwent preoperative electrophysiologic study unless he or she was in hemodynamically unstable condition and had clinically documented ventricular tachycardia before operation. Operative survivors underwent postoperative electrophysiological testing usually 1 week after operation. Surgical failure was determined by a positive electrophysiologic study revealing sustained monomorphic ventricular tachycardia. The study was considered positive even if the ventricular tachycardia had a different morphology or rate than the initial presenting arrhythmia.

Operative Technique

The technique has been previously described [4]. In brief, all patients were anesthetized with narcotics and placed on normothermic cardiopulmonary bypass (38° to 40°C) before induction of VT. Repeat cycles of sequential mapping and resection or cryoablation (R. Wallach cryoprobe, Milford, CT) or both were performed until no further VT could be induced during the operation. The operative time for this portion of the procedure was limited to approximately 60 minutes or less if possible. After mapping and resection, the aorta was cross-clamped, systemic hypothermia was induced (28°C), and crystalloid car-

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Kron, Department of Surgery, University of Virginia Health Sciences Center, Box 310, Charlottesville, VA 22908.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Patient Characteristics

Aneurysm Location	No. of Patients	Age (y)	Sex (M/F)	No. of Antiarrhythmic Drugs	Recent MI (%)[a]	Preop Ejection Fraction
Anterior	96	60 ± 1	49/47	1.9 ± 0.2	43	0.31 ± 0.01
Posterior	14	62 ± 2	8/6	1.9 ± 0.4	36	0.37 ± 0.04

[a] This is an MI within 8 weeks before operation.

MI = myocardial infarction.

dioplegia was given if concomitant coronary artery bypass grafting or mitral valve replacement was required. If only left ventricular aneurysm resection was performed, the patient was maintained on normothermic bypass, and no cross-clamp was used. When VT could not be induced in the operating room, an extended subendocardial resection of all visible scar was done followed by attempts to restart the arrhythmia after the resection.

In the posterior aneurysm or infarct group, if the VT was localized to the septum, then endocardial resection was performed on the septum with no manipulation of the papillary muscles. However, if the VT was localized to the papillary muscles, two techniques of therapy were used. Usually in this situation, the papillary muscles were resected and the mitral valve replaced through the aneurysm or infarct [6]. In three instances, cryoablation of the posterior papillary muscle was performed with particular attention paid to the annular isthmus as described by Hargrove and associates [7].

Statistical Analysis

Unpaired data were compared by t test and χ^2 analysis when appropriate. Significance was achieved when the p value was less than 0.05. Survival curves were created by the technique of Kaplan and Meier.

Results

There were few clinical differences between the two groups. Preoperative left ventricular ejection fraction was not significantly different between the posterior and anterior groups (0.37 ± 0.04 versus 0.31 ± 0.01, respectively).

Operative survival was not significantly different between the two groups: 94% for the anterior group versus 100% for the posterior group (Table 2). Mitral valve replacement was required in 6% of the anterior group versus 29% of the posterior group ($p \leq 0.05$). Eleven percent of the anterior group had a positive postoperative electrophysiologic study compared with 14% of the posterior group (p = not significant). The 5-year survival rate for the anterior group was 76% ± 5% versus 77% ± 14% for the posterior group (Fig 1).

Table 2. Operative Results[a]

Aneurysm Location	Operative Survival	Positive Postop EP Study	MVR	5-Year Survival (%)
Anterior	90/96 (94)	10/90 (11)	6/96 (6)	76 ± 5
Posterior	14/14 (100)	2/14 (14)	4/14 (29)[b]	77 ± 14

[a] Numbers in parentheses are percentages. [b] Significance: $p \leq 0.05$ versus anterior group by χ^2 analysis.

EP = electrophysiologic study; MVR = mitral valve replacement.

In the group with posterior aneurysm or infarct, 7 had the VT localized to the septum and underwent successful endocardial resection. Seven had the tachycardia localized to the posterior papillary muscles. Four were treated with mitral valve replacement after papillary muscle resection, and the surgical intervention was successful in all 4. Three others had the arrhythmia localized to the posterior papillary muscle, and it was thought that the arrhythmia could be controlled medically if necessary. For this reason, extensive cryoablation of the posterior papillary muscle and posterior annulus was performed. In 2 of these patients, the VT was reinducible at postoperative electrophysiological testing.

Comment

Endocardial resection for VT has been less successful when there is an inferior scar. Saksena and co-workers [8] noted a similar mortality rate among patients with an anterior versus posterior anatomic location (7% versus 10%, respectively). However, the postoperative electrophysiologic study was positive in 15% with anterior infarcts versus 67% of those with posterior infarcts. Ostermeyer and colleagues [9] noted that the lack of an

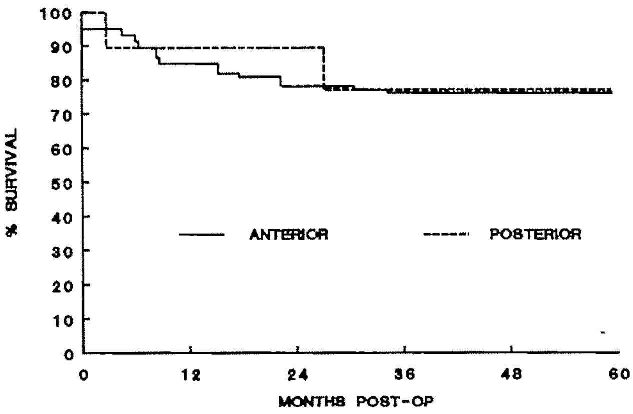


Fig 1. Kaplan-Meier survival curves for the group with an aneurysm in the anterior location and that with an aneurysm or infarct in the posterior location.

anterior aneurysm was a predictor of decreased 5-year survival. The 5-year survival rate was 31% when there was no anterior aneurysm present compared with 86% when there was an anterior aneurysm. Posterior wall resection was a constant phase hazard [9]. Yee and co-authors [10] confirmed these findings and suggested the automatic internal cardioverter defibrillator as a palliative alternative for patients with less favorable infarct location.

Many techniques have been developed for the treatment of ventricular tachycardia resulting from a scarred posterior papillary muscle. We [6] previously have taken a relatively aggressive approach to this clinical situation in advocating papillary muscle resection and mitral valve replacement. Ivey [11], Moran [12], and their associates agreed with this approach and have reported relatively good results, particularly in patients with mappable arrhythmias. Landymore and colleagues [13] suggested partial reimplantation of the papillary muscle or, in some cases, encircling endocardial ventriculotomy when the entire papillary muscle was involved. Cox and co-workers [14] also advocated encircling endocardial ventriculotomy when a posterior papillary muscle was involved.

Several authors have suggested cryoablation as an alternative. Caceres and associates [15] suggested cryoablation alone. This technique was used in 15 patients with only one death. However, 3 of the 14 surviving patients did have a positive postoperative electrophysiologic study. Hargrove and co-authors [7] indicated that the annular isthmus is a critical component of the reentrant circuit in these tachycardias. They compared two groups of patients with posterior infarcts and VT. Group I underwent standard subendocardial resection with four operative deaths (13%), and ventricular tachycardia was inducible in 44% of the survivors. In group II, the technique of annular cryoablation was performed in addition to subendocardial resection with one operative death (7%), and 13 of 14 survivors (93%) had no inducible ventricular tachycardia at postoperative electrophysiologic study. We tried this technique in 3 patients, but it was successful in only 1.

Recently, Svenson and colleagues [16] suggested the use of both endocardial and epicardial laser photocoagulation. They reported that 35 patients underwent this technique with an overall mortality rate of 14%. Of the 30 survivors, 14 had circumflex coronary artery infarcts, and 9 of these patients had epicardial photocoagulation alone. Only 3 of the 30 survivors had a positive postoperative electrophysiologic study or clinical recurrence of VT. This technique does sound intriguing, but certainly further work will have to be done to determine who can undergo epicardial photocoagulation alone.

We noted better results than we would initially have predicted in patients with ventricular tachycardia related to a posterior location. Long-term survival and VT ablation as noted by postoperative electrophysiologic study were equivalent to the findings in the anterior group. We speculate that the failures in the posterior group could have been circumvented by posterior papillary muscle resection. The issue is whether or not a posterior papillary muscle resection and mitral valve replacement is better than placement of an implantable defibrillator or long-term drug therapy. We are not certain of the answer. Clearly, an implantable defibrillator is an excellent alternative to subendocardial resection in select patients [17]. The trouble is that concomitant drug therapy is often required.

We suggest that in patients who have a posterior aneurysm and have failed initial drug therapy, an aggressive surgical approach should be used. If the ventricular tachycardia is mapped to the septum, the decision in the operating room is easy, and endocardial resection can be performed without difficulty. On the other hand, if the ventricular tachycardia is mapped to the posterior papillary muscle, the decision is more difficult. If the preoperative arrhythmia is particularly frequent and poorly controlled by drugs, posterior papillary muscle resection and mitral valve replacement is in order. If the presenting arrhythmia is easily controlled or infrequent, the surgeon could decide to leave the papillary muscles intact, attempt cryoablation, and hope for the best. In this latter group, we suggest the placement of prophylactic defibrillator patches because this group is very likely to have a positive postoperative electrophysiological study. However, defibrillator placement could easily be accomplished at a later date should it be necessary. Despite this one caveat, the posterior aneurysm or infarct is certainly not a contraindication to endocardial resection. In our series, the results are essentially equivalent to those in patients with an anterior aneurysm.

References

1. Horowitz LN, Harken AH, Kastor JA, Josephson ME. Ventricular resection guided by epicardial and endocardial mapping for treatment of recurrent ventricular tachycardia. N Engl J Med 1980;302:589–93.
2. Hammon JW Jr, Echt DS, Merrill WH, et al. Indications for different modes of surgical therapy in medically refractory ventricular arrhythmias. Ann Surg 1986;203:679–84.
3. Miller JM, Kienzle MG, Harken AH, Josephson ME. Subendocardial resection for ventricular tachycardia: predictors of surgical success. Circulation 1984;70:624–31.
4. Kron IL, Lerman BB, Nolan SP, Flanagan TL, Haines DE, DiMarco JP. Sequential endocardial resection for the surgical treatment of refractory ventricular tachycardia. J Thorac Cardiovasc Surg 1987;94:843–7.
5. Kron IL, Haines DE, Tribble CG, et al. Operative risks of the implantable defibrillator versus endocardial resection. Ann Surg 1990;211:600–4.
6. Kron IL, DiMarco JP, Lerman BB, Nolan SP. Resection of scarred papillary muscles improves outcome after surgery for ventricular tachycardia. Ann Surg 1986;203:685–90.
7. Hargrove WC III, Miller JM, Vassalo JA, Josephson ME. Improved results in the operative management of ventricular tachycardia related to inferior wall infarction. J Thorac Cardiovasc Surg 1986;92:726–32.
8. Saksena S, Hussain SM, Wasty N, Gielchinsky I, Parsonnet V. Long-term efficacy of subendocardial resection in refractory ventricular tachycardia: relationship to site of arrhythmia origin. Ann Thorac Surg 1986;42:685–9.
9. Ostermeyer J, Borggrefe M, Breithardt G, et al. Direct operations for the management of life-threatening ischemic ventricular tachycardia. J Thorac Cardiovasc Surg 1987;94:848–65.
10. Yee ES, Schienman MM, Griffin JC, Ebert PA. Surgical

options for treating ventricular tachyarrhythmia and sudden death. J Thorac Cardiovasc Surg 1987;94:866–73.
11. Ivey TD, Brady GH, Misbach GA, Greene HL. Surgical management of refractory ventricular arrhythmias in patients with prior inferior myocardial infarction. J Thorac Cardiovasc Surg 1985;89:369–77.
12. Moran JM, Kehoe RF, Loeb JM, et al. The role of papillary muscle resection and mitral valve replacement in the control of refractory ventricular arrhythmia. Circulation 1983;68:154–60.
13. Landymore RW, Kinley CE, Gardner M. Encircling endocardial resection with complete removal of endocardial scar without intraoperative mapping for the ablation of drug-resistant ventricular tachycardia. J Thorac Cardiovasc Surg 1985;89:18–24.
14. Cox JL, Gallagher JJ, Ungerleider RM. Encircling endocardial ventriculotomy for refractory ischemic ventricular tachycardia. J Thorac Cardiovasc Surg 1982;83:865–72.
15. Caceres J, Werner P, Jazayeri M, Akhtar M, Tchou P. Efficacy of cryosurgery alone for refractory monomorphic sustained ventricular tachycardia due to inferior wall infarction. J Am Coll Cardiol 1988;11:1254–9.
16. Svenson RH, Littmann L, Gallagher JJ, et al. Termination of ventricular tachycardia with epicardial laser photocoagulation: a clinical comparison with patients undergoing successful endocardial photocoagulation alone. J Am Coll Cardiol 1990;15:163–70.
17. Hargrove WC III, Josephson ME, Marchlinski FE, Miller JM. Surgical decisions in the management of sudden cardiac death and malignant ventricular arrhythmias. J Thorac Cardiovasc Surg 1989;97:923–8.

DISCUSSION

DR HOOSHANG BOLOOKI (Miami, FL): Dr Kron, I have been following your excellent work and support the hypothesis presented here. My colleagues and I do some work similar to yours, and have practically abandoned subendocardial resection for two reasons. First, I was never convinced that the procedure eliminated the danger of sudden death. Second, with this operation, I think we render the left ventricular wall, especially the septum, very soft and therefore dyskinetic. If we perform this procedure, we place a large patch over the septum to give it enough strength to prevent paradoxical motion.

I have two questions. What if you were to do cryoablation only and not papillary muscle resection, especially on the posterior wall? Do you believe the area of early activation is within the papillary muscle itself, or do you think it is in the wall of the left ventricle?

Our 6-year study involves some 59 patients. We have found that if we could successfully map the tachycardia, we did not have to use the automatic implantable cardioverter defibrillator (AICD) in about 80% of the patients. Have you had to use an AICD for any patient whose arrhythmia was not inducible initially after the operation but became inducible 2 or more years later? This situation has affected 2 of our 59 patients, or 4%.

DR KRON: Dr Bolooki, I have seen your results, and they are excellent. We take no issue with how you want to eliminate the arrhythmia. Cryoablation, laser ablation, or anything you can do that is reproducible is fine with us. We have not had very good results in our own series with just cryoablation on the papillary muscles. Before we did the sequential resection, we tried cryoablation different ways as we have been doing it in the laboratory, and we could not predictably ablate the arrhythmia. There are people who say they can, and more power to them. In Charlottesville, Virginia, we cannot.

The second question concerns the late use of AICDs. To date, we have not had to add an AICDs at a later date. If the patient had a negative study, we have seen very little recurrence of a ventricular arrhythmia, and we have not had to use AICDs in this group of patients.

DR JOHN W. HAMMON JR (Winston-Salem, NC): That was a very nice report, and I thank you for sharing the manuscript with me before the presentation. Like you, I believe that if the papillary muscles are involved, mitral valve replacement should be done. However, my approach differs slightly from yours. Our two series are now about the same size.

My associates and I initially had poor results with arrhythmia control in patients with a posterior aneurysm when we were trying to do endocardial resection and cryoablation. I think many of these posterior aneurysms are relatively localized. They are confluent with the base of the heart and often involve the mitral apparatus. If the intention is to leave the mitral apparatus intact, we have had good results doing a rather limited encircling endocardial ventriculotomy right around the aneurysm posteriorly and then using cryoablation at the bases of the papillary muscles if they are not involved. If the patient has mitral regurgitation and papillary muscle dysfunction preoperatively, it makes a lot more sense to us to go ahead and resect the mitral valve.

DR KRON: I appreciate your kind comments, Dr Hammon. You and I have been following each other's series for a long time. Your approach is similar to that of Dr Cox, ie, a limited encircling endocardial ventriculotomy around the base of the papillary muscle. I guess I have never had the courage to try that. My fear has been that it would fall apart on me. However, if indeed it is successful, it is a worthwhile thing to do. I am also fearful about the long-term results in terms of blood supply to the papillary muscle. This may not be an issue, but it does trouble me. Therefore, we have opted for the more radical approach.

DR GORDON N. OLINGER (Milwaukee, WI): This concept is based on the premise that you can induce ventricular tachycardia and map it in the operating room. What do you do when you have opened a posterior aneurysm or infarct and are unable to get a satisfactory map?

DR KRON: That is an excellent question, but I was hoping I was not going to be asked that today. We have had a real preference for the anterior location, and the patients we have seen with the posterior location have had fairly virulent arrhythmias. They have been very inducible and were easily mapped in the operating room. In fact, to date, we have not had a patient in the posterior group in whom mapping could not be done. If we had that circumstance and clinically the arrhythmia was malignant, I think the correct approach includes resection of the papillary muscles, cryoablation on the septum, and mitral valve replacement. If the patient has concomitant ventricular tachycardia but really needs a coronary bypass procedure, then you can take an approach that is a little bit more conservative and leave the papillary muscles alone. It really depends on just how life-threatening the arrhythmia is, and that is how we would approach it.

Anomalous Left Coronary Artery From the Pulmonary Artery: Results of Isolated Aortic Reimplantation

Pascal R. Vouhé, MD, Daniel Tamisier, MD, Daniel Sidi, MD, Françoise Vernant, MD, Philippe Mauriat, MD, Philippe Pouard, MD, and Francine Leca, MD

Laënnec Hospital, Paris V University, Paris, France

Thirty-one consecutive children with anomalous left coronary artery underwent direct aortic reimplantation of the anomalous artery without an associated procedure. There were five deaths (16%; 70% confidence limits, 9% to 26%), three in the hospital and two early (within 3 months). The severity of preoperative left ventricular dysfunction was the only incremental risk factor for mortality: 31% mortality rate among patients with left ventricular shortening fraction of less than 0.20 versus 0% among patients with a left ventricular shortening fraction of 0.20 or more ($p = 0.03$). There were no late deaths up to 6 years, a survival rate of 84% ± 7%. Late results were studied in 23 survivors having a follow-up of longer than 12 months. Ninety-six percent were free of symptoms; left ventricular function recovered to normal in all patients; moderate to severe mitral regurgitation decreased to minimal or no regurgitation in most patients (5/7); and the reimplanted anomalous left coronary artery was patent in each patient. Based on this study, we reached five conclusions. (1) Direct aortic reimplantation is technically feasible in most patients with anomalous left coronary artery and yields a high rate of late patency. (2) Left ventricular resection is unnecessary. (3) The mitral valve should not be interfered with at the initial operation, but mitral regurgitation may persist in a few patients and necessitate later operation. (4) In patients with moderate left ventricular dysfunction, the operative risk is low and early operation indicated. (5) In patients with severe left ventricular dysfunction, the operative risk is high; heart transplantation may be suggested, but our current approach favors an immediate corrective procedure.

(Ann Thorac Surg 1992;54:621–7)

An anomalous left coronary artery (ALCA) arising from the pulmonary artery is a rare congenital cardiac malformation that carries a very poor natural prognosis, particularly in symptomatic infants [1, 2]. A number of surgical procedures have been advocated in the past, but there is now general agreement that the restoration of a two-vessel coronary artery system is desirable [2–7]. However, controversy persists regarding the optimal surgical management (technique of revascularization of the ALCA, need for associated procedures) and the ideal timing of operation.

Since 1983, all children with ALCA seen at our institution underwent a uniform surgical approach using direct aortic reimplantation of the ALCA without an associated procedure (resection of left ventricular myocardium or mitral valve repair). The early and late results obtained in this consecutive series were evaluated.

Material and Methods

Patient Population

Thirty-one consecutive children with ALCA underwent isolated aortic reimplantation of the anomalous artery between April 1983 and July 1991. There were 16 boys and 15 girls. The mean age at operation was 16 ± 19 months (± the standard deviation) (range, 2 to 90 months).

Indications for operation evolved over time. In the early part of the series, the operative risk of immediate surgical intervention was considered very high, and the policy was to delay such intervention, particularly in symptomatic infants. Since the late 1980s, operation has been performed as soon as the diagnosis is made. Therefore the patients were divided into three groups according to the preoperative clinical status and the timing of operation.

Preoperative clinical data are summarized in Table 1. Seventeen patients (55%) had no or minimal congestive heart failure under adequate medical treatment and underwent elective operation at a mean age of 23 ± 23 months (range, 3 to 90 months). Fourteen patients (45%) had persistent symptoms of congestive heart failure despite aggressive medical therapy. Six of these children underwent delayed operation, the mean interval between diagnosis and operation being 10 ± 5 months (range, 1 to 15 months). The other 8 infants underwent immediate

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Prof Vouhé, Department of Cardiovascular Surgery, Laënnec Hospital, 42, rue de Sèvres, 75340 Paris Cedex 07, France.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Preoperative Clinical Data[a,b]

Group	No. of Patients	Age (mo)	Weight (kg)	CT ratio	Mitral Insufficiency[c]			SF	
					0/+	++	+++	Mean	<0.20
No or minimal CHF	17	23 ± 23	10.7 ± 6.4	0.64 ± 0.06	15	1	1	0.23 ± 0.07	5 (29)
Persistent CHF	14	7 ± 6	5.7 ± 2.2	0.73 ± 0.06	9	3	2	0.13 ± 0.05	11 (79)
Delayed operation	6	11 ± 7	7.1 ± 2.7	0.76 ± 0.06	5	1	0	0.14 ± 0.05	4 (67)
Immediate operation	8	4.5 ± 2	4.7 ± 0.9	0.72 ± 0.05	4	2	2	0.12 ± 0.04	7 (87.5)
Total	31	16 ± 19	8.4 ± 5.5	0.68 ± 0.07	24 (77)	4 (13)	3 (10)	0.19 ± 0.08	16 (52)

[a] Where applicable, data are shown as the mean ± the standard deviation. [b] Numbers in parentheses are percentages. [c] Mitral insufficiency was graded as follows: 0/+ = none or mild; ++ = moderate; +++ = severe.

CHF = congestive heart failure; CT = cardiothoracic; SF = shortening fraction.

operation; 2 were receiving mechanical ventilation and intravenous inotropic support.

Surgical Management

All patients underwent direct aortic reimplantation of the ALCA with hypothermic cardiopulmonary bypass.

After a transverse incision was made in the pulmonary trunk, the left coronary ostium was precisely identified. As suggested by Smith and associates [8], the pulmonary sinuses were designated as right-hand, left-hand, and nonfacing according to the view obtained from the nonfacing pulmonary sinus looking toward the aorta. In most patients (26/31), the ALCA originated from the right-hand pulmonary sinus. In 5, the origin of the ALCA was more unusual: left-hand pulmonary sinus (1), above the commissure between the right-hand and nonfacing sinuses (1), posterior aspect of the right pulmonary artery near its origin (2), and posterior aspect of the left pulmonary artery near its origin (1).

The division of the pulmonary trunk was completed, with the incision allowing a sizable button of pulmonary artery wall around the left coronary ostium to be excised (Fig 1A). The left main coronary artery was mobilized up to its bifurcation. Venous collaterals around the artery usually required careful control. The aortic and pulmonary roots were dissected apart down to the pulmonary annulus. An opening was made in the adjacent left-sided wall of the ascending aorta, with care taken to avoid valve leaflet damage. The button around the coronary ostium was anastomosed to the aorta with an 8-0 absorbable running suture (Fig 1B). Mobilization of the pulmonary bifurcation and division of the ligamentum arteriosum allowed end-to-end reconstruction of the pulmonary trunk in most patients. However, when compression of the reimplanted ALCA was feared, a patch of fresh autologous pericardium was used to close the defect created in the pulmonary wall by the excision of the coronary ostium (Fig 1C).

Very careful attention was paid to intraoperative myocardial preservation, although the method of protection changed over time. Multidose crystalloid cardioplegia was used initially and then replaced by multidose blood car-

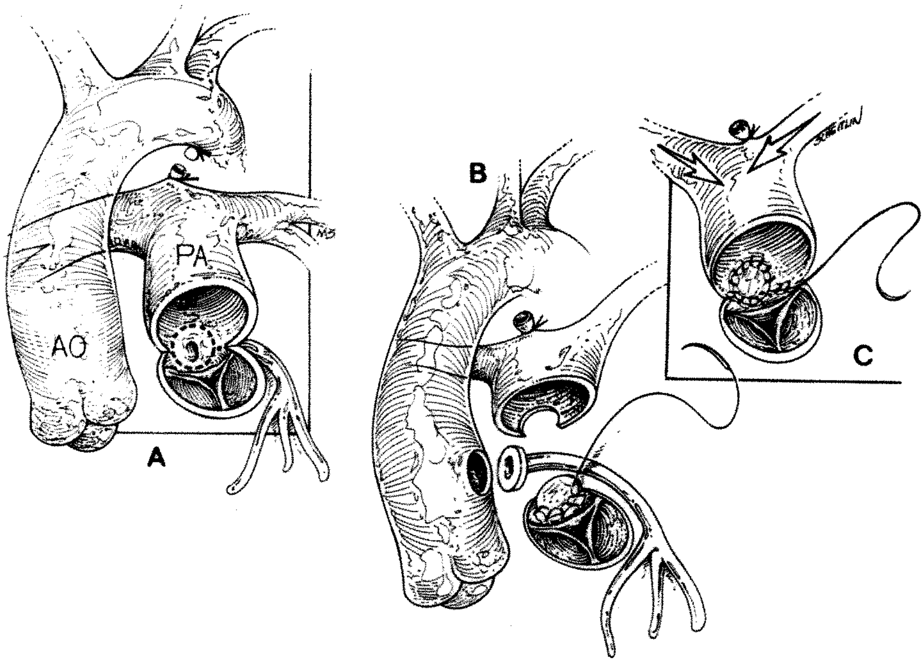


Fig 1. Surgical technique: (A) excision of the left coronary ostium; (B) aortic reimplantation of the coronary ostium; and (C) reconstruction of the pulmonary trunk. (AO = aorta; PA = pulmonary artery.)

dioplegia. The current technique, including multidose blood cardioplegia and warm blood cardioplegic reperfusion, has been in use since 1988. After aortic cross-clamping, a cold blood cardioplegic solution was infused into the ascending aorta with digital occlusion of the origin of the ALCA. Cardioplegia infusion was repeated directly into the coronary ostium as soon as the left coronary artery was identified, and again into the ascending aorta after completion of the reimplantation. Before the aorta was unclamped a reperfusate, aspartate/glutamate–enriched warm blood cardioplegic solution, was administered.

In all patients, isolated reimplantation of the ALCA was performed. Infarcted left ventricular myocardium was not resected. The mitral valve was not repaired even when regurgitation was judged moderate or severe.

Results

Operative Results

Nine patients (29%) were easily weaned from cardiopulmonary bypass and had an uneventful postoperative course.

In the other 22 patients (71%), left atrial–aortic partial bypass was instituted either because left atrial pressure was high (>15 mm Hg) at the end of the operation (16 patients) or because preoperative left ventricular function was severely depressed (6 patients). Mean left atrial pressure before bypass was 18 ± 3 mm Hg (± the standard deviation) (range, 10 to 25 mm Hg). The mean duration of left heart assistance was 94 ± 59 minutes (range, 30 to 240 minutes). All patients were finally weaned from bypass. In most patients (18/22, 82%), left atrial pressure decreased significantly and at the end of bypass was less than 15 mm Hg (mean pressure, 13 ± 2 mm Hg); all these patients survived the immediate postoperative period. In 4 patients, left atrial pressure remained greater than 15 mm Hg (mean pressure, 17.5 ± 1 mm Hg) despite prolonged left heart assistance (mean duration, 165 ± 57 minutes); 3 of these infants died of low cardiac output syndrome shortly after operation.

Early Results

EARLY MORTALITY. Five patients (16%; 70% confidence limits, 9% to 26%) died early. Three of them (10%; 70% confidence limits, 4% to 18%), just mentioned, died of untractable low cardiac output syndrome; postmortem examination showed a patent reimplantation and marked left ventricular dilatation with severe endocardial and papillary muscle fibrosis. Two patients (6%; 70% confidence limits, 2% to 14%) died after discharge. One died 3 weeks postoperatively of severe pulmonary infection; the reimplanted ALCA was patent at postmortem examination. The other died suddenly at home 2 months after operation, presumably of cardiac rhythm disorder; left ventricular function was still severely depressed (shortening fraction, 0.14); postmortem examination was not done.

INCREMENTAL RISK FACTORS FOR MORTALITY. Potential risk factors were evaluated: date of operation, age at operation, presence of persistent congestive heart failure, timing of operation in patients with persistent congestive heart failure, presence of mitral regurgitation, and severity of left ventricular dysfunction (Table 2). Only the last factor significantly increased the operative risk: mortality rate of 31% (5/16) (70% confidence limits, 18% to 47%) among patients with left ventricular shortening fraction of less than 0.20 versus 0% mortality rate (0/15) (70% confidence limits, 0% to 12%) among patients with left ventricular shortening fraction of 0.20 or greater.

EARLY COMPLICATIONS. Low cardiac output syndrome necessitating pharmacological support for more than 48 hours occurred in 18 operative survivors (64%). Other complications included mediastinitis (1) and transient hemiplegia caused by a cerebral embolus from a left ventricular thrombus (1).

Late Results

There were no late deaths, a survival rate of 84% ± 7% (± the standard error) (Fig 2). All 26 survivors were followed up (mean follow-up, 4.4 ± 2.5 years [± the standard deviation]; range, 5 months to 8.75 years). Three patients had a follow-up of less than 1 year, and the long-term effects of operation could not be assessed adequately; therefore, the late results were evaluated in the 23 survivors with a follow-up of more than 1 year (mean follow-up, 4.9 ± 2.2 years [± the standard deviation]).

FUNCTIONAL STATUS. All patients but 1 (22/23, 96%) were free of symptoms and leading a normal life without cardiac medication. One patient remained in functional class II 6.5 years postoperatively because of severe residual mitral regurgitation, even though global left ventricular function had returned to normal.

LEFT VENTRICULAR FUNCTION. Global left ventricular function, assessed by left ventricular shortening fraction measured at echocardiography, improved in each patient (Fig 3). Mean left ventricular shortening fraction increased from 0.19 ± 0.08 (± the standard deviation) preoperatively to 0.36 ± 0.05 postoperatively ($p < 0.001$). At last examination, the shortening fraction was within normal range (≥0.30) in all patients.

MITRAL REGURGITATION. Seven patients had moderate to severe mitral insufficiency preoperatively. At last follow-up, the severity of regurgitation decreased to none or mild in 5 patients but remained unchanged in 2 (moderate in 1, severe in 1). In these 2 patients, the valvular insufficiency was tolerated well and did not require further operation.

PATENCY OF THE REIMPLANTED ALCA. Eight patients underwent cineangiography 2 to 6 years postoperatively. In each, the left coronary artery was patent and without stenosis (Fig 4). In all the other long-term survivors, echocardiography with Doppler color-flow imaging

Table 2. Risk Factors for Mortality

Risk Factor	No. of Patients	Mortality No.	Mortality %	Mortality CL	p Value[a]
Date of operation					
1983–1985	8	1	12.5	2%–36%	
1986–1988	13	2	15	5%–33%	NS
1989–1991	10	2	20	7%–41%	
Age at operation (mo)					
0–12	18	3	17	8%–30%	
12–24	7	2	29	10%–55%	NS
>24	6	0	0	0%–27%	
CHF					
Absent or minimal	17	1	6	1%–19%	0.15
Persistent	14	4	29	15%–45%	
Timing of operation in patients with CHF					
Delayed operation	6	2	33	12%–62%	NS
Immediate operation	8	2	25	9%–50%	
Mitral insufficiency					
None or mild	24	5	21	12%–32%	0.56
Moderate or severe	7	0	0	0%–24%	
LV shortening fraction					
≥0.20	15	0	0	0%–12%	0.03
<0.20	16	5	31	18%–47%	

[a] The p value was obtained with Fisher's exact text.

CHF = congestive heart failure; CL = 70% confidence limits; LV = left ventricular; NS = not significant.

showed a patent left coronary artery. Overall, the patency rate was 100%.

SUPRAVALVULAR PULMONARY STENOSIS. In 1 patient, there was a mild residual gradient (25 mm Hg) across the reconstructed main pulmonary artery.

Comment

Restoration of a two-vessel coronary artery system in patients with ALCA can be achieved by a number of methods. Aortocoronary bypass using either a saphenous vein graft [9] or a free segment of subclavian artery [2] is an unsatisfactory procedure in infants because of the risk of occlusion or progressive stenosis caused by lack of growth potential. Left subclavian–left coronary artery anastomosis is an attractive procedure, as it can be performed without the need for cardiopulmonary bypass and aortic cross-clamping [6, 7, 10]. However, the risk of occlusion and the tendency for the left subclavian artery to kink at its origin remain unsolved difficulties. Intrapulmonary tunnel repair using a pulmonary artery flap [11], a free segment of subclavian artery [2], or a polytetrafluoroethylene baffle [3] is considered the procedure of choice in many surgical centers. Nevertheless, there remains a risk of tunnel occlusion, aortic valve damage at the time of the creation of the aortopulmonary window, and acquired supravalvular pulmonary stenosis [3]. Anatomical correction of the malformation by direct aortic reimplantation of the ALCA [12] has been used in several series, but it is not usually considered the optimal procedure. It is said that the procedure is technically difficult and that it is often not possible to obtain a sufficient length of left main coronary artery to transplant it onto the aorta without undue tension, which can compromise patency.

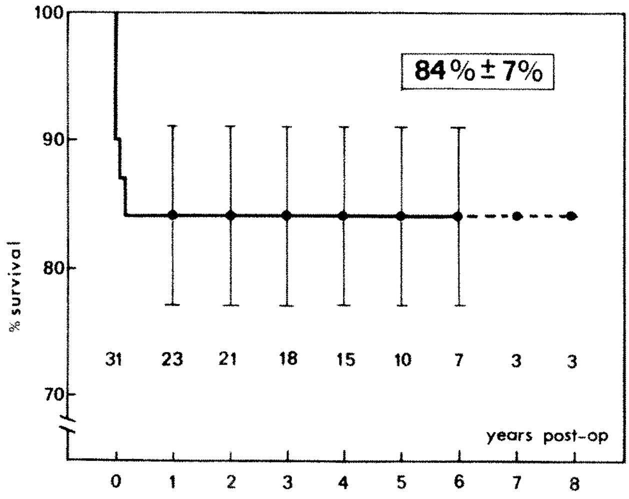


Fig 2. Actuarial survival (± the standard error).

Anatomical studies [8] showed that the ALCA usually originates from the so-called right-hand pulmonary sinus, an anatomical situation that allows easy direct aortic reimplantation. The origin of the ALCA was more uncommon in 5 patients in the present series; nevertheless, direct aortic reimplantation was performed without specific surgical difficulty. This may be explained by several

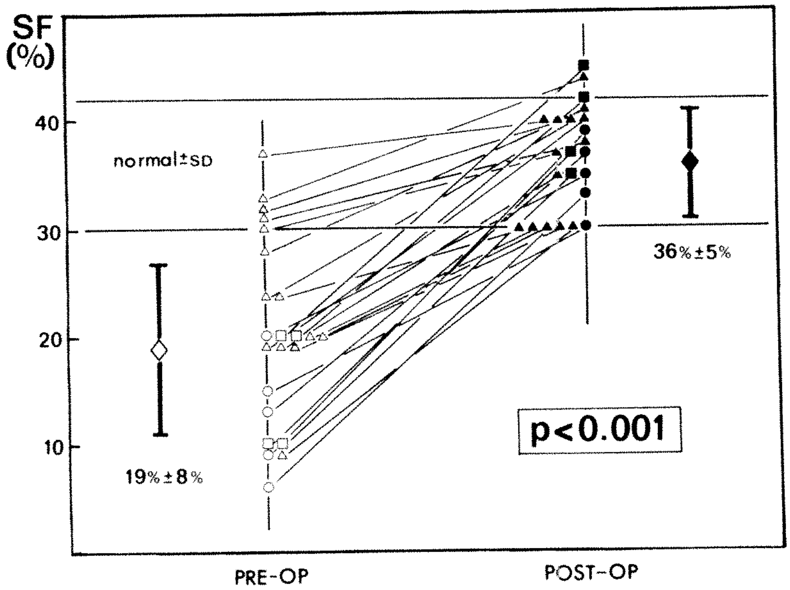


Fig 3. Left ventricular shortening fraction (SF) before (open symbols) and after (solid symbols) operation. (SD = standard deviation; triangles = patients without congestive heart failure [CHF]; squares = patients with CHF undergoing delayed operation; circles = patients with CHF undergoing immediate operation.)

factors: elasticity of infant tissues, generous excision of the pulmonary arterial wall surrounding the coronary ostium (in effect, excised pulmonary wall becomes the proximal left coronary artery and thus elongates the vessel), and extensive experience with the arterial switch procedure for transposition of the great arteries. Even in the more unfavorable anatomical situation (anomalous origin from the nonfacing pulmonary sinus), technical modifications using pulmonary arterial and aortic flaps have been designed to allow aortic reimplantation of the ALCA [13]. As shown in the present series, direct aortic reimplantation yields a high rate of late patency (100%); this represents a very strong argument in favor of the procedure. Aortic reimplantation is currently our procedure of choice; it is probably technically feasible in almost all infants with ALCA, and intrapulmonary tunnel repair may be indicated only in the very few patients in whom coronary arterial transfer seems impossible.

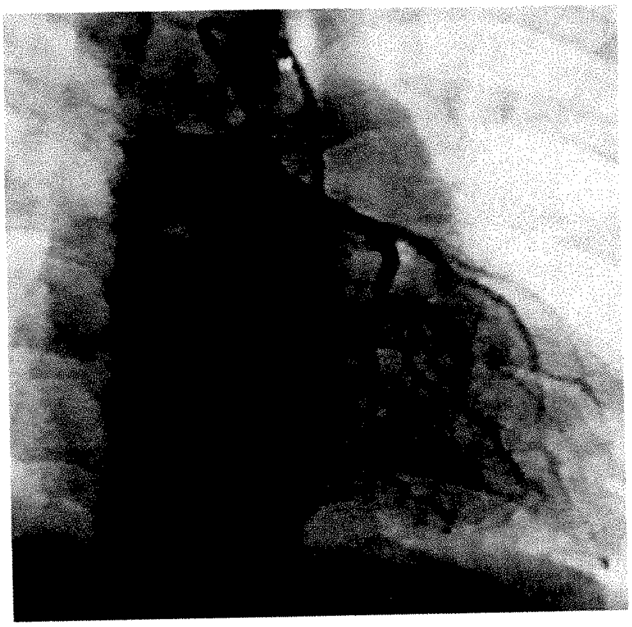


Fig 4. Left coronary angiogram made 5 years after direct aortic reimplantation.

It has been clearly documented that the successful restoration of a two-vessel coronary artery system provides marked improvement in left ventricular function [2–7, 14]. In the present series, all late survivors recovered normal global left ventricular function as assessed by shortening fraction measured at echocardiography. This suggests that even severely damaged myocardium has a great potential for recovery, presumably because there are ischemic viable myocardial cells scattered throughout the scarred ventricle. Consequently, surgical excision of left ventricular myocardium is not required.

Mitral insufficiency is a very common finding in infants with ALCA, although the severity of the valvular regurgitation varies considerably. Valvular insufficiency is related both to the effects of left ventricular dilatation on mitral valve function and to ischemic damage to the papillary muscles. For several reasons, the mitral valve should not be interfered with at the initial operation: (1) Mitral regurgitation almost always lessens after successful revascularization of the ALCA, as this restores normal left ventricular function and improves papillary muscle function in patients with reversible ischemic damage. (2) Repairing the mitral valve in infancy can be difficult and can increase the overall operative risk. (3) As shown in the present series, the presence of moderate to severe mitral insufficiency does not increase the risk of isolated revascularization of the ALCA (there was no mortality among patients with moderate or severe mitral regurgitation). However, in a few patients, mitral regurgitation caused by irreversible ischemic damage to the mitral valve apparatus can persist after successful revascularization. Further surgical intervention can be required occasionally. Mitral valvuloplasty can then be performed with a low operative risk in an older child with normal left ventricular function.

There are two subsets of infants with ALCA. In some patients, intercoronary collateral circulation develops early, and only mild to moderate myocardial damage results. These patients usually become free of symptoms with medical therapy. As shown in the present series, the operative risk of corrective intervention is very low. Early operation (within a few weeks) is indicated to provide early complete recovery of left ventricular function.

In other infants, intercoronary collaterals do not develop early, and severe myocardial damage results. These infants usually have persistent symptoms of congestive heart failure despite medical therapy. Simple ligation of the ALCA in this situation carries a very high operative risk [2, 3]. Delaying coronary revascularization, the usual recommendation in the past, is also hazardous; the risk of premature death (sudden death or chronic congestive heart failure) is high during the waiting period [5, 15]. An aggressive surgical approach is therefore mandatory.

Heart transplantation may be suggested and has actually been performed in a few instances. The early risk is relatively low, but the long-term results in terms of mortality and morbidity remain unknown. The results of coronary revascularization are diametrically opposite: the early risk remains high (31% early morbidity rate in our series), but the late results are very satisfactory (no late deaths, recovery of normal left ventricular function in all patients). Unless the late results of pediatric heart transplantation prove very successful, which seems unlikely [16–18], early coronary revascularization remains the procedure of choice in the treatment of these very sick infants.

Urgent operation is indicated, and the recommendation that operation be delayed is no longer tenable. Delaying operation does not decrease the operative risk and may even decrease the rate and amount of improvement in left ventricular function [4, 5]. Immediate operation is therefore indicated to avoid further ischemic damage to the left ventricle and maximize its potential for functional recovery. The operative risk remains high and is clearly related to the severity of the preoperative myocardial damage. Improved intraoperative management may yield a further decrease in the early risk of operation. The current technique of myocardial preservation, including multidose blood cardioplegia and warm blood cardioplegic reperfusion, may benefit from further refinements. Left heart assistance using extracorporeal membrane oxygenation was liberally used in the present series, but only for limited periods. The use of refined mechanical devices may allow a longer time of left heart assistance and thus decrease the operative risk in patients with severely depressed left ventricular function.

We express our appreciation to Corinne Pasquet for secretarial assistance.

References

1. Wesselhoeft H, Fawcett JS, Johnson AL. Anomalous origin of the left coronary artery from the pulmonary trunk: its clinical spectrum, pathology and pathophysiology, based on a review of 140 cases with seven further cases. Circulation 1968;38:403–25.
2. Arciniegas E, Farooki ZQ, Hakimi M, Green EW. Management of anomalous left coronary artery from the pulmonary artery. Circulation 1980;62(Suppl 1):180–9.
3. Bunton R, Jonas RA, Lang P, Rein AJJT, Castaneda AR. Anomalous origin of left coronary artery from pulmonary artery. Ligation versus establishment of a two coronary artery system. J Thorac Cardiovasc Surg 1987;93:103–8.
4. Vouhé PR, Baillot-Vernant F, Trinquet F, et al. Anomalous left coronary artery from the pulmonary artery in infants. Which operation? When? J Thorac Cardiovasc Surg 1987;94:192–9.
5. Kakou-Guikahue M, Sidi D, Kachaner J, et al. Anomalous left coronary artery arising from the pulmonary artery in infancy: is early operation better? Br Heart J 1988;60:522–6.
6. Kesler KA, Pennington DG, Nouri S, et al. Left subclavian–left coronary artery anastomosis for anomalous origin of the left coronary artery. Long-term follow-up. J Thorac Cardiovasc Surg 1989;98:25–9.
7. Montigny M, Stanley P, Chartrand C, Selman E, Fournier A, Davignon A. Postoperative evaluation after end-to-end subclavian–left coronary artery anastomosis in anomalous left coronary artery. J Thorac Cardiovasc Surg 1990;100:270–3.
8. Smith A, Arnold R, Anderson RH, et al. Anomalous origin of the left coronary artery from the pulmonary trunk. Anatomic findings in relation to pathophysiology and surgical repair. J Thorac Cardiovasc Surg 1989;98:16–24.
9. El-Said GM, Ruzyllo W, Williams RL, et al. Early and late results of saphenous vein graft for anomalous origin of the left coronary artery from the pulmonary artery. Circulation 1973;48(Suppl 3):2–9.
10. Meyer BW, Stefanik G, Stiles QR, Lindesmith GG, Jones JC. A method of definitive surgical treatment of anomalous origin of left coronary artery. J Thorac Cardiovasc Surg 1968;56:104–7.
11. Takeuchi S, Imamura H, Katsumoto K, et al. New surgical method for repair of anomalous left coronary artery from pulmonary artery. J Thorac Cardiovasc Surg 1979;78:7–11.
12. Neches WH, Mathews RA, Park SC, et al. Anomalous origin of the left coronary artery from the pulmonary artery: a new method of surgical repair. Circulation 1974;50:582–7.
13. Sese A, Imoto Y. New technique in the transfer of an anomalously originated left coronary artery to the aorta. Ann Thorac Surg 1992;53:527–9.
14. Rein AJJT, Colan SD, Parness IA, Sanders SP. Regional and global left ventricular function in infants with anomalous origin of the left coronary artery from the pulmonary trunk: preoperative and postoperative assessment. Circulation 1987;75:115–23.
15. Driscoll DJ, Nihill MR, Mullins CE, Cooley DA, McNamara DG. Management of symptomatic infants with anomalous origin of the left coronary artery from the pulmonary artery. Am J Cardiol 1981;47:642–8.
16. Pahl E, Fricker FJ, Armitage J, et al. Coronary arteriosclerosis in pediatric heart transplant survivors: limitation of long-term survival. J Pediatr 1990;116:177–83.
17. Addonizio LJ, Hsu DT, Smith CR, Gersony WM, Rose EA. Late complications in pediatric cardiac transplant recipients. Circulation 1990;82(Suppl 4):295–301.
18. Vouhé PR, Tamisier D, Leca F, et al. Heart transplantation in children: risk factors of early and late mortality. Eur J Cardio-thorac Surg 1991;5:176–82.

DISCUSSION

DR JAN M. QUAEGEBEUR (New York, NY): Dr Vouhé, I rise to congratulate you for this very nice presentation and work on a difficult group of patients. There is almost nothing in this presentation with which I can disagree. We follow the same concepts and we agree that very sick patients should be taken to the operating room as soon as possible, and you should have some sort of left ventricular assist device ready in case you need it.

I have one question. In your experience there is apparently a group of patients in whom you delay the operation until a new age of, I believe, 11 months. How do you make the decision to delay repair of anomalous coronary artery from the pulmonary artery, once you have made the diagnosis?

DR VOUHÉ: The present consecutive series is extending over an 8-year period, and our indications in symptomatic infants have changed with time. At the beginning of the series, operation was delayed because the risk of immediate operation was considered to be too high. On the contrary, our current policy is to perform immediate operation in all symptomatic infants.

DR ADNAN COBANOGLU (Portland, OR): I congratulate Dr Vouhé and associates for an excellent series and one of the largest that I am aware of with so many anomalous coronary arteries. We certainly agree with their policy of operating early. These infants usually are very sick in the neonatal intensive care unit or pediatric intensive care units, on drips, drugs, ventilators, and other support systems. So I think early operation should be one of the main principles in treating this problem.

The question that I have is related to the intraoperative management. I think that trying to pull the anomalous coronary ostium to the aorta in every case may be more of an emotional and technical exercise than something that is absolutely necessary. In the last 6 or 7 years in Portland we have adopted the technique described by Dr Takeuchi. We make a connection between the ascending aorta and the pulmonary artery, and we use a 4- or 5-mm coronary punch to make the holes and the anastomosis; then, using the anterior wall of the pulmonary artery as baffle material, we direct blood to the coronary ostium. In our experience this procedure has been very adequate, the ventricular function has been excellent 6 months down the line, almost uniformly, and we have not had to undertake tedious dissection around the coronary artery and risk distortion or kinking of the vessel.

DR VOUHÉ: It is well known that the Takeuchi operation is the procedure of choice in many pediatric surgical centers. I have no personal experience with this procedure. However, I would like to point out that direct aortic reimplantation of an anomalous left coronary artery is really not a very demanding surgical procedure. It is very similar to coronary artery transfer during the arterial switch operation for transposition of the great arteries.

DR HILLEL LAKS (Los Angeles, CA): I also congratulate you on your excellent results and big experience. We used to use the Takeuchi procedure and now use this. I would like to emphasize also the use of left ventricular assistance, which particularly seems to help these patients rather than other children with isolated left ventricular assistance using the centrifugal pump. We have had 2 patients, both of whom were on inotropes and in cardiogenic shock, who recovered, and at 1 year their ventricular function was completely normal. So I think, particularly in the very young ones, heart transplantation is probably not a very good option, particularly in view of the difficulty of getting it done immediately, whereas in the older ones who are in more stable condition, closer to a year of age, it could be considered.

One other technical detail that I learned from Dr Yacoub is that rather than doing the anastomosis in the back of the aorta, one can make a transverse incision in the front of the aorta and make an opening in the sinus, pull the button into the aorta, and do the anastomosis from inside of the aorta, that technical modification is very easy to do, there is no bleeding, and it avoids sewing in the back of the aorta. I do not know if you have had experience with that.

DR VOUHÉ: I do agree with you regarding the usefulness of left ventricular assistance in this group of patients. I believe that the use of refined methods of left heart assistance should minimize the risk of operation in these very sick infants.

DR ERIC L. CEITHAML (Jacksonville, FL): We also agree with early operative intervention in these patients, but we have had occasion to see 1 or 2 older children who had extensive right to left collaterals and seemed to have either congenital or acquired stenosis of the left main coronary artery. These patients were generally asymptomatic and had good left ventricular function. Have you had any experience with older children with anomalous left coronary arteries like this with stenosis at the pulmonary origin, and how would you deal with these patients?

DR VOUHÉ: It is true that older children may have well-preserved left ventricular function. Nevertheless, I believe that it is preferable to restore a two-vessel coronary artery system to prevent sudden death, a complication that has been described after simple ligation of the anomalous left coronary artery.

DR JOHN W. HAMMON, JR (Winston-Salem, NC): Dr Vouhé, I think a parallel can be drawn perhaps in the group of patients who had the highest mortality, the ones with the poorest left ventricular function, and those patients who do not do well in some cases after a coronary reimplantation and the switch procedure; those are the patients in whom dilated ventricle does develop, for whatever reason. I wonder if the reason why temporary left heart assist does not work in this group of patients is because it decompresses the left ventricle and takes the stretch off the reimplanted coronary artery.

Also, Dr Jacobs wanted me to ask you, in your group of patients who died, were the coronary anastomoses patent or did you have any evidence in the postoperative period that more myocardial ischemia developed during times of ventricular distention?

DR VOUHÉ: In the 3 patients who died early, postmortem examination showed a patent reimplanted left coronary artery. I have the impression that persistent left ventricular dysfunction was related more to the severity of the preoperative myocardial ischemic damage than to the presence of stretching of the reimplanted artery because of ventricular distention.

Anterior Mediastinal Tracheostomy With and Without Cervical Exenteration

Mark B. Orringer, MD

Section of Thoracic Surgery, Department of Surgery, The University of Michigan Medical Center, Ann Arbor, Michigan

Anterior mediastinal tracheostomy (AMT) facilitates resection of stomal recurrences after laryngectomy for carcinoma and tumors involving the cervicothoracic trachea and esophagus. Erosion of the innominate artery has been reported as a frequent major complication of AMT, and routine prophylactic division of the innominate artery with AMT has even been advised. Forty-four patients underwent AMT, 10 as an isolated procedure (for stomal recurrence [5], laryngeal carcinoma [1], or benign stenosis after laryngectomy [4]) and 34 with concomitant cervical exenteration (laryngopharyngoesophagectomy) for laryngeal, thyroid, or cervicothoracic esophageal malignancies. Transposition of the remaining tracheal stump beneath and to the right of the innominate artery to eliminate tension on the vessel was carried out in 14 patients (32%). Postoperatively, anastomotic leaks complicated nine of 31 pharyngogastric anastomoses. Iatrogenic hypoparathyroidism occurred in 10 patients. All six hospital deaths (14%) occurred in patients undergoing AMT with cervical exenteration, not isolated AMT. There was only one instance of innominate artery erosion. Survival was related to the pathology for which AMT was performed. Anterior mediastinal tracheostomy is a valuable adjunct in the treatment of select patients with malignancies of the cervicothoracic trachea and esophagus, and with attention to operative detail, innominate artery erosion should rarely, if ever, complicate the operation. Prophylactic division of the innominate artery with AMT is unnecessary.

(Ann Thorac Surg 1992;54:628–37)

The need to divide the high retrosternal trachea poses a formidable surgical problem, as it may be impossible to elevate the remaining trachea sufficiently out of the superior mediastinum and over the upper sternum for construction of a standard tracheostome in the suprasternal notch. There are nonetheless a number of clinical situations in which division of the retrosternal trachea is required: localized tracheal stomal recurrence after a prior laryngectomy for carcinoma; extensive thyroid or laryngeal carcinomas involving the upper trachea; and hypopharyngeal, postcricoid, and cervicothoracic esophageal carcinomas that invade the upper trachea.

Removal of the anterior upper thoracic "breastplate" (the medial clavicles, manubrium, and portions of the adjacent first and second costal cartilages) unroofs the superior mediastinum and provides unequaled exposure to its contents, the intrathoracic trachea, and the cervicothoracic esophagus. With the bony anterior thorax so removed, the overlying skin drops into the anterior mediastinum to meet the trachea, which has been divided within centimeters of the carina. Thus, rather than attempting to pull the end of the divided trachea up and over the sternum to reach the cervical skin, the surgeon brings the skin of the upper anterior thorax into the mediastinum for construction of an anterior mediastinal tracheostomy. The magnitude of this operation is compounded by the need for a concomitant laryngopharyngectomy and reestablishment of alimentary continuity. The addition of a transhiatal esophagectomy without thoracotomy and esophageal substitution using either the transposed stomach or colon anastomosed to the pharynx is an effective option in the patient requiring such cervical exenteration: removal of the larynx, proximal trachea, pharynx, and esophagus.

Erosion of the innominate artery has been among the gravest complications reported after anterior mediastinal tracheostomy, and prophylactic division of this vessel, the interposition of rotated muscle flaps between the trachea and the innominate artery, and omental flaps have been used to minimize this occurrence. Alternatively, the technique of tracheal transposition beneath and to the right of the innominate artery eliminates any tension on this vessel.

This report reviews my experience with anterior mediastinal tracheostomy performed both with and without cervical exenteration. By compulsive avoidance of any tension between the trachea, the skin, and the adjacent innominate artery, neither prophylactic innominate artery division nor routine use of rotated mediastinal muscle or omental flaps is required in construction of an anterior mediastinal tracheostomy.

Material and Methods

During the past 13 years, 44 patients (35 men and 9 women) ranging in age from 42 to 77 years (average age, 61 years) have undergone anterior mediastinal tracheostomy on the Thoracic Surgery Service at The University

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Orringer, Section of Thoracic Surgery, The University of Michigan Medical Center, 1500 E Medical Center Dr, Ann Arbor, MI 48109.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

of Michigan Medical Center. A retrospective review of the records of these patients was performed.

Ten patients underwent an isolated anterior mediastinal tracheostomy: 5 for stomal recurrence after laryngectomy for squamous cell carcinoma, 1 for laryngeal recurrence after a prior hemilaryngectomy for carcinoma, and 4 for benign stomal stenosis after laryngectomy and radiation therapy for laryngeal carcinoma. Nine of these 10 patients had received prior radiation therapy for their primary tumors. Thirty-four patients underwent anterior mediastinal tracheostomy with concomitant cervical exenteration (pharyngoesophagectomy, usually also with laryngectomy): 20 for postcricoid or cervicothoracic esophageal squamous cell carcinoma; 6 for pharyngeal or hypopharyngeal squamous cell carcinoma, 4 with recurrence after prior laryngectomy for carcinoma; 5 for locally advanced laryngeal squamous cell carcinoma; 2 for thyroid carcinoma; and 1 for a high malignant tracheoesophageal fistula. Nineteen had received prior radiation therapy for their primary tumors.

Weight loss in the 26 patients with esophageal obstruction ranged from 4.5 to 18 kg (10 to 40 pounds) (average loss, 10.35 kg [23 pounds]). None of the patients with carcinoma had demonstrable distant metastatic disease. Preoperative mediastinal and tracheal laminagrams were used initially to evaluate the size and position of the tumor mass and to rule out extensive paratracheal adenopathy that might preclude resection and construction of a mediastinal tracheostomy. During the past 10 years, the computed tomographic scan has been relied on more heavily for evaluating mediastinal adenopathy. However, as a minimum 5-cm tumor-free length of distal trachea is optimal for construction of a mediastinal tracheostomy, careful preoperative bronchoscopy and precise measurement of the distance from the carina to the tumor are critical.

Lack of fixation of the tumor to the prevertebral fascia and ability to obtain minimum gross tracheal and esophageal mucosal margins of resection of 1.5 cm beyond the tumor are determined at operation before initiation of major resection and anterior mediastinal tracheostomy. The discovery of innominate artery or aortic arch invasion by tumor in the superior mediastinum precludes resection and anterior mediastinal tracheostomy. The involved common carotid artery can be resected with the tumor, preferably after preoperative angiographic and hemodynamic measurements indicating adequate remaining cerebral blood flow are obtained. Two patients in this series, 1 with thyroid cancer and 1 with laryngeal cancer, underwent resection of involved common carotid artery with resultant transient hemiplegia that resolved within 7 to 14 days.

In the 34 patients undergoing anterior mediastinal tracheostomy and concomitant cervical exenteration, the transhiatal approach was used in each to resect the esophagus, and esophageal substitution was achieved with either the stomach (31) or colon (3), the latter group including 2 patients who had undergone a prior gastric resection for peptic ulcer disease.

A bipedicled upper thoracic apron flap was used to construct the mediastinal tracheostomy in 17 patients, an extended collar incision alone in 15, and a thoracoacromial "nipple" rotational flap in 12 in whom there was a need to resurface the anterior neck after resection of skin involved with tumor. Transposition of the remaining tracheal stump beneath and to the right of the innominate artery to eliminate tension on the vessel was carried out in 14 patients (32%), 4 undergoing isolated anterior mediastinal tracheostomy and 10 having combined anterior mediastinal tracheostomy and cervical exenteration. In 3 patients, one or two of the resected parathyroid glands were identified and reimplanted into pectoralis major muscle, avoiding late iatrogenic hypoparathyroidism.

Operative Technique

My technique of anterior mediastinal tracheostomy has been described previously [1] but has been refined over the past decade. The patient is positioned supine with the neck extended by means of a folded blanket beneath the shoulders. The head is stabilized on a head ring. As for a transhiatal esophagectomy, the operative field extends from the mandibles to the pubis and laterally to the midaxillary lines. The bipedicled upper thoracic "visor" flap originally described by Grillo [2] is no longer used, and it is therefore unnecessary to prepare the anterior thigh as a possible skin-graft donor site. (For patients in whom a thoracoacromial flap is required, a split-thickness skin graft can be harvested from the lower abdomen if necessary.) Unless there is a need to resect anterior cervical skin involved by tumor, anterior mediastinal tracheostomy and cervical exenteration including laryngopharyngectomy can be performed through an extended collar incision, essentially a long transverse supraclavicular incision (Fig 1). Elevation of a flap of anterior cervical skin and platysma to the level of the hyoid bone provides ample exposure for later resection of the larynx and construction of the pharyngeal anastomosis.

In patients with tumors involving the cervicothoracic esophagus but not the anterior cervical skin, beginning on the side most involved by tumor, the anterior border of the sternocleidomastoid muscle and the carotid sheath are mobilized and retracted laterally and the trachea and thyroid medially. The dissection is carried directly posteriorly through the cervical fascial planes to the prevertebral fascia. Mobility of the tumor away from the carotid vessels and lack of prevertebral fascial invasion are established as blunt finger dissection proceeds downward along the prevertebral fascia into the superior mediastinum and upward behind the pharynx. The opposite side of the neck is explored in similar fashion, and resectability of the tumor is established. If the location of the tumor necessitates a laryngectomy, and if the inferior extent involves the cervicothoracic esophagus or trachea within or below the thoracic inlet so that division of the retrosternal trachea will be required, the decision for anterior mediastinal tracheostomy is made.

The needle-tipped electrocautery is used to elevate skin and subcutaneous fat from the pectoralis major muscle fascia inferiorly. To achieve the exposure necessary for resection of the upper anterior chest wall, the skin over-

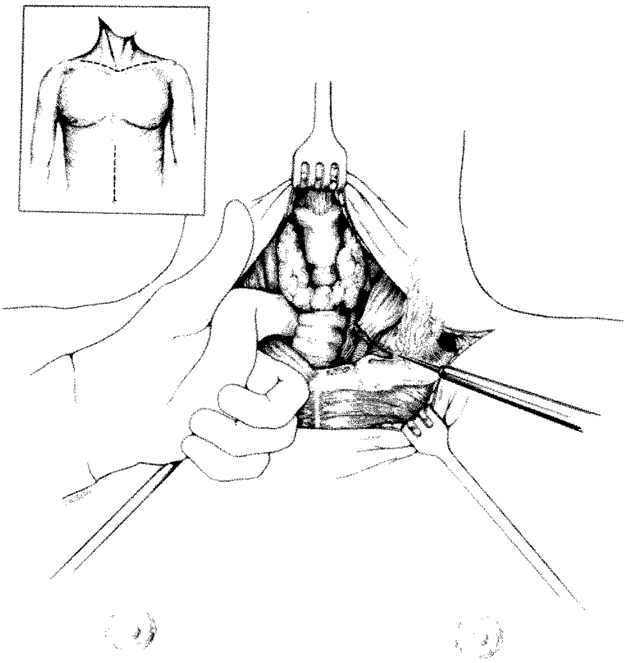


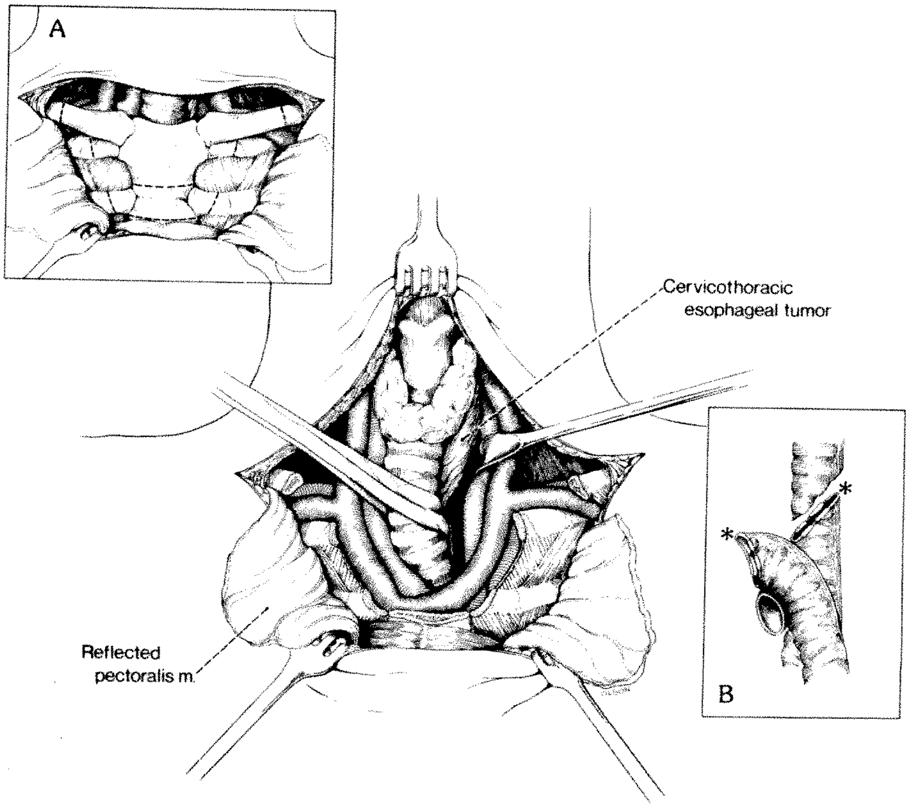
Fig 1. Anterior mediastinal tracheostomy: initial approach. Inset *shows the extended supraclavicular collar incision used. Once it is established that the cervicothoracic esophageal tumor is free from the carotid sheaths and paravertebral fascia, the anterior cervical skin and platysma are elevated and the sternocleidomastoid muscles detached from their sternal and clavicular attachments. The bipedicled upper thoracic visor flap of Grillo [2] is no longer used. (Modified with permission from Orringer MB, Sloan H. Anterior mediastinal tracheostomy. J Thorac Cardiovasc Surg 1979;78:850–9.)*

lying the upper sternum, medial clavicles, and first and second costal cartilages must be elevated (Fig 2). This may require vigorous downward retraction of the skin and temporary flexion of the neck to permit relaxation and elevation of the skin. However, such traction is considered preferable to the second transverse anterior thoracic incision of the Grillo bipedicled flap, and avoidance of another incision leaves better-vascularized skin for later construction of the tracheostome.

The insertions of the sternocleidomastoid and strap muscles onto the sternum and clavicles are divided, and the high retrosternal space is developed by blunt finger dissection during which the pleural reflections are gently swept laterally. Pectoralis major fascia is divided in the midline with cautery from the suprasternal notch to the sternomanubrial junction (the second intercostal space), and the pectoralis major muscles are elevated from the chest wall bilaterally, exposing the clavicles, manubrium, and first and second costal cartilages (see Fig 2). Carefully so as not to injure the subclavian vessels, each clavicle is encircled and divided approximately 4 to 6 cm from the sternoclavicular joint. The tough ligamentous attachments between the divided medial clavicle and subadjacent first rib are incised with heavy scissors until the upper edge of the first rib can be felt.

The subclavian vessels are displaced laterally as the tip of the electrical sternal saw is positioned against the upper border of the first rib. Positive endotracheal pressure is temporarily interrupted by the anesthetist to permit the lungs to drop away from the chest wall, and the first rib is

Fig 2. Anterior mediastinal tracheostomy: resection of anterior thoracic breastplate. Excellent exposure of the superior mediastinum, the thoracic trachea, and cervicothoracic esophagus is achieved. (Inset A) Incision through the medial thirds of the clavicles, adjacent first costal cartilages, and sternum above *the sternomanubrial junction* (upper dotted line*). For very low tracheal division, the second costal cartilages and sternum* below *the sternomanubrial junction* (lower dotted line*) are resected. (Inset B) Oblique division of the trachea is required to allow the posterior membranous portion to reach the skin when the trachea is brought forward over the innominate artery. (Modified with permission from Orringer MB, Sloan H. Anterior mediastinal tracheostomy. J Thorac Cardiovasc Surg 1979;78:850–9.)*



divided with the saw, which is advanced downward and medially through the first rib and across the sternum, usually just above the sternomanubrial junction (see Fig 2, inset A). The saw is removed and repositioned in the same fashion on the opposite side, and resection of the anterior breastplate is completed. Division of the second costal cartilage and sternal division at or below the sternomanubrial junction may be performed if it is anticipated that very distal division of the trachea will be required (see Fig 2, inset A). Protection of the subclavian vessels during resection of the anterior breastplate is important if major hemorrhage is to be avoided. Further, if the retrosternal soft tissues are not adequately mobilized and swept laterally before the chest wall resection is begun with the sternal saw, injury to one or both internal thoracic arteries may also cause untoward bleeding.

This "unroofing" of the anterior thoracic inlet provides exposure of the retrosternal trachea, cervicothoracic esophagus, and adjacent superior mediastinal lymph nodes (see Fig 2). The thymus, adjacent mediastinal fat, and superior mediastinal lymph nodes are mobilized superiorly with the specimen after the innominate vessels have been identified and protected. The adventitia surrounding the innominate artery should *not* be dissected from the vessel, as skeletonizing the innominate artery only increases the risk of subsequent erosion. *The innominate artery is not divided in construction of the anterior mediastinal tracheostomy.* The plane between the trachea and esophagus distal to palpable tumor is developed, and the trachea is encircled at this point with a rubber drain. When a concomitant esophagectomy is to be performed, the esophagus is also encircled with a rubber drain at the same level.

Through an upper midline abdominal incision, gastric mobilization, pyloromyotomy, Kocher maneuver, and feeding jejunostomy are performed, and transhiatal esophageal mobilization, as described previously [3, 4], is carried out, facilitated by traction and blunt dissection of the esophagus encircled in the superior mediastinum. When a transhiatal esophagectomy is performed in a patient undergoing concomitant laryngopharyngectomy, the *lower* end of the esophagus is divided with the GIA stapler, and a Penrose drain is sutured to the esophagus. The esophagus is then mobilized out of the chest and into the neck wound, drawing the attached drain up through the posterior mediastinum in the esophageal bed. The drain is used for later repositioning of the stomach. (In dividing the esophagogastric junction, it is important that no squamous epithelium be left attached to the stomach to avoid later occult ulceration and bleeding.)

Distal tracheal mobilization is performed only anteriorly and posteriorly to the trachea to minimize the risk of devascularization from injury to the lateral blood supply. The trachea is divided obliquely, the posterior membranous portion being left longer than the anterior cartilaginous edge (see Fig 2, inset B), because once the remaining trachea is bent forward for construction of the tracheostome, the membranous edge must reach most anteriorly. Excessive trauma and fragmentation of the tracheal cartilages must be avoided. As the trachea is divided, the oral endotracheal tube is gradually withdrawn, and the distal trachea is intubated across the field with a flexible armored endotracheal tube, which is sutured to the edge of the trachea to avoid inadvertent displacement of the tip of the tube down one main bronchus. Back in the abdomen, the tip of the gastric fundus that will reach most superiorly is sutured to the distal end of the previously positioned Penrose drain in the esophageal bed, and the stomach is advanced through the posterior mediastinum and delivered into the neck wound. The presence of the stomach within the thoracic inlet minimizes later mediastinal contamination once the pharynx is divided and opened.

For the majority of tumors involving the cervicothoracic esophagus, posterior pharynx, or upper trachea, a narrow-field laryngectomy is adequate: the thyrohyoid membrane is entered just above the thyroid cartilage, the laryngeal and pharyngeal mucosa is divided by carrying the incision laterally and posteriorly, and the hyoid bone is left behind. The epiglottis is grasped, retracted downward, and amputated, and its base is oversewn with running 2-0 chromic catgut suture. Whenever possible, consistent with achieving an adequate margin of resection, one or both lobes of the thyroid gland and its adjacent parathyroid glands should be preserved. Alternatively, identification and resection of one or two parathyroid glands with gentle mincing and reimplantation into the exposed pectoralis major muscle may prevent long-term postoperative iatrogenic hypoparathyroidism.

The resected cervical exenteration specimen includes the larynx (if a prior laryngectomy has not already been performed), proximal trachea, pharynx, adjacent mediastinal fat and lymph nodes, and the attached thoracic esophagus. The pharyngogastric anastomosis is performed with a single layer of interrupted 3-0 polyglycolic acid suture. The anastomosis is marked with silver clips for later roentgenographic follow-up and is covered with either adjacent pharyngeal muscle or omental fat left attached to the high gastric fundus in the process of gastric mobilization. A 10-mm Jackson-Pratt drain is placed on either side of the anastomosis and is brought out through a stab wound above the level of the clavicles. The mobilized pectoralis major muscle is allowed to fall back over the cut edges of the sternum and first and second ribs (Fig 3, inset A).

The tracheostome is generally incorporated directly into the cervical incision as the wound is closed. Careful approximation of tracheal mucosa and cervical skin is important. Interrupted 3-0 polyglycolic acid suture is used for this. Occasionally it is necessary to place the stoma several centimeters inferior to the neck incision by excising a 1.5- to 2-cm button of skin, temporarily removing the endotracheal tube, bringing the trachea through the skin opening, and reintubating the trachea. As the end of the trachea is brought anteriorly and approximated to the skin, it must be determined if there is any tension against the innominate artery. If there is, the space beneath and to the right of the innominate vessels is developed bluntly, the endotracheal tube is temporarily removed, the trachea is repositioned beneath the innominate artery,

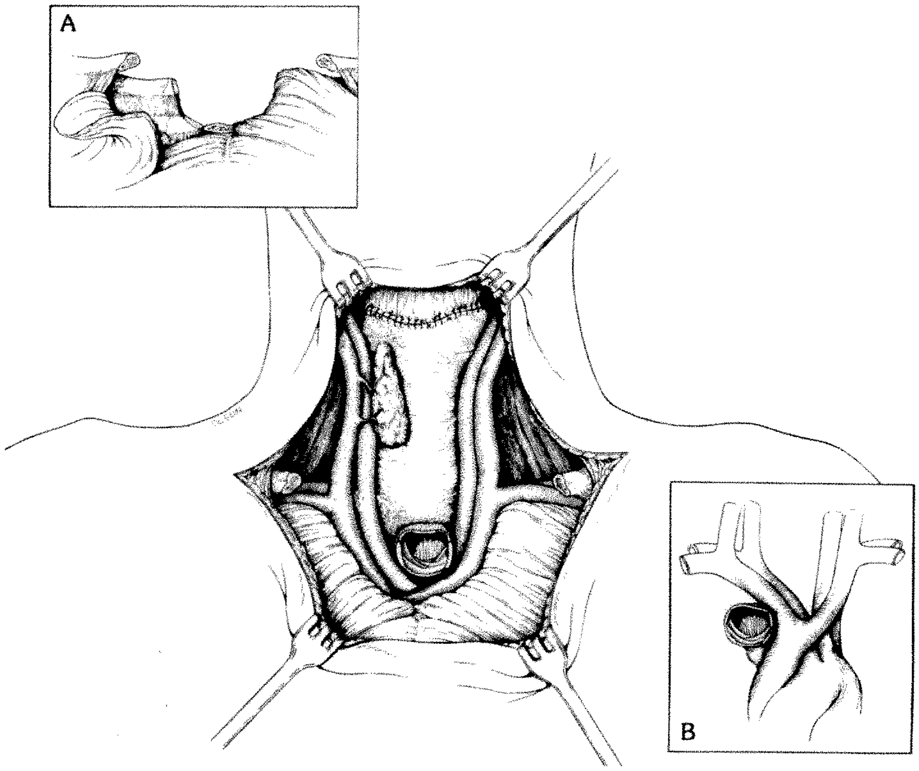


Fig 3. Completion of pharyngogastric anastomosis and final positioning of trachea. (Inset A) The reflected pectoralis major muscle is allowed to fall back into the mediastinum over the cut edges of the bony chest wall. Whenever possible, a lobe of the thyroid gland is preserved. The divided end of the trachea is brought forward over the innominate artery for construction of the tracheostome. (Inset B) If there is the least bit of pressure on the innominate artery by the overlying trachea, transposition of the end of the trachea below and to the right of the innominate artery eliminates tension on the vessel when the trachea is sutured to the skin. (Modified with permission from Orringer MB, Sloan H. Anterior mediastinal tracheostomy. J Thorac Cardiovasc Surg 1979;78:850–9.)

and the endotracheal tube is reinserted (Fig 3, inset B). This maneuver of tracheal transpositioning permits elevation of an additional 1.5 to 2 cm of the end of the trachea out of the mediastinum for skin suturing and completely eliminates the risk of later pressure erosion of the innominate artery by the adjacent trachea.

In patients with tracheal stomal recurrence after prior laryngectomy or a malignant pharyngocutaneous fistula above an established tracheostome, a wide portion of anterior cervical skin must be excised en bloc with the specimen (Fig 4B, 4C). In such situations, a thoracoacromial or nipple flap is used to resurface the anterior neck and mediastinum. Resectability of the tumor is determined through incisions that can be incorporated to define a 3- to 5-cm margin around the stoma and involved skin. The thoracoacromial flap of skin and subcutaneous tissue is elevated off pectoralis muscle on the side from which the most cervical skin must be removed. The flap is outlined by a supraclavicular incision that curves downward in the midline over the sternum and then laterally in the inframammary crease, preserving a pedicle 10 to 15 cm wide from the anterior shoulder and the thoracoacromial nourishing vessels (see Fig 4B, 4C). The anterior breastplate is removed, and the stoma, surrounding skin, and adjacent several centimeters of retrosternal trachea are resected. A pharyngoesophagectomy, if necessary, is performed.

After the completion of the pharyngogastric anastomosis, the thoracoacromial flap is rotated superiorly and medially over the anterior neck and mediastinum, and the tracheostome is constructed, with the same criteria being used to establish the need for tracheal transposition beneath the innominate artery as described already. The trachea is sutured to the skin, the incision is closed over wound catheters, and the remaining anterior thoracic skin

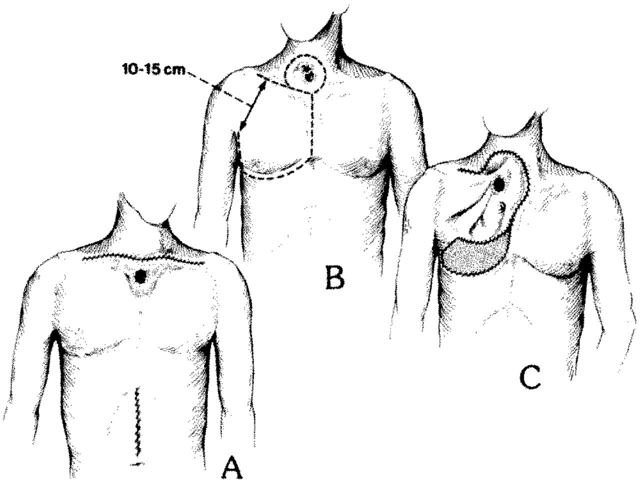


Fig 4. (A) Extended collar incision, anterior mediastinal tracheostomy, and upper midline abdominal incision after cervical exenteration, transhiatal esophagectomy, and pharyngogastric anastomosis. The tracheostome can often be incorporated into the cervical incision as it is closed rather than creating a separate opening on the upper thoracic skin flap as shown. (B) Incisions used to resect tracheal stomal recurrence and skin involved with tumor and the thoracoacromial "nipple" flap for reconstruction. (C) Rotated thoracoacromial flap in position, mediastinal tracheostomy, and skin-grafted anterior thorax. (Modified with permission from Orringer MB, Sloan H. Anterior mediastinal tracheostomy. J Thorac Cardiovasc Surg 1979;78:850–9.)

defect is covered with a split-thickness skin graft harvested from the lower abdomen (see Fig 4C).

Intraoperative and Postoperative Management

As is standard in the performance of transhiatal esophagectomy without thoracotomy, intraarterial blood pressure is monitored through a radial artery catheter to prevent prolonged hypotension from displacement during dissection of the thoracic esophagus. Oxygen saturation is monitored to ensure adequate oxygenation after the trachea has been divided and during repositioning of the endotracheal tube. Jugular or subclavian intravenous catheters are generally avoided, as they interfere with the operative field, and two large-bore peripheral intravenous lines for fluid and blood replacement are more than adequate. A portable chest roentgenogram is obtained in the operating room at the conclusion of the operation to assess chest tube position, rule out an unrecognized pneumothorax or hemothorax, and document satisfactory position of the tip of the endotracheal tube in the short length of remaining trachea above the carina.

Postoperative mechanical ventilation is seldom required after isolated mediastinal tracheostomy, but when a concomitant laryngopharyngoesophagectomy has been performed, ventilatory assistance for 24 to 48 hours is advised. Maintaining the position of the endotracheal tube above the carina is critical and can be challenging when only a short length of trachea remains [1]. Trauma to the trachea must be minimized by use of as low a pressure as possible in the endotracheal tube balloon. Regurgitation, particularly during endotracheal tube suctioning and coughing, is common early after a pharyngogastric anastomosis in which both esophageal sphincters have been sacrificed. This can be disastrous if gastric contents flow out of the mouth, over the chin, and down into the mediastinal tracheostome. Therefore, nasogastric tube decompression of the intrathoracic stomach is continued, at times for a week or more, until the patient is ambulatory and can sit up while coughing.

Iatrogenic hypoparathyroidism is diagnosed by routine serial calcium determinations postoperatively and is treated initially with intravenous calcium and later with long-term oral calcium and vitamin D supplementation. Although the jejunostomy feeding tube placed at operation provides an excellent means for early postoperative caloric intake, calcium replacement must be given either intravenously or orally, as the majority of calcium absorption takes place in the duodenum.

Results

Morbidity and Mortality

There were six hospital deaths among the 44 patients, a 14% mortality rate. They were due to innominate artery erosion (1), cerebrovascular accident (1), acute myocardial infarction (1), anastomotic leak and sepsis (1), renal and respiratory insufficiency (1), and hepatorenal syndrome (1). All six deaths occurred in the group of 34 patients undergoing anterior mediastinal tracheostomy and concomitant cervical exenteration, not the group having isolated anterior mediastinal tracheostomy.

Among the 28 hospital survivors of anterior mediastinal tracheostomy and concomitant cervical exenteration, postoperative complications included pharyngeal anastomotic leak (6), iatrogenic hypoparathyroidism and hypothyroidism (9), cerebrovascular accident (3), cervical chyle fistula (3), delayed splenic rupture (1), and hepatic failure caused by cirrhosis (1). Only 9 (32%) of the 28 patients had a completely uncomplicated postoperative course. The duration of hospitalization after combined anterior mediastinal tracheostomy and cervical exenteration ranged from 10 to 51 days (average time, 26.2 days), and only 4 (14%) of the surviving patients were discharged within 2 weeks after operation. Twenty-one (75%) of the 28 surviving patients were discharged between 22 and 51 days after operation.

An anastomotic leak complicated nine of the 31 pharyngogastric anastomoses but was relatively transient, responding to local drainage, in all but 2 patients. An anastomotic leak in a patient who had had extensive cervical radiation therapy for his primary tumor resulted in sepsis that ultimately caused the patient's death. Necrosis of the upper 3 cm of the gastric pull-up developed in 1 patient and ultimately necessitated a free jejunal graft to bridge the resulting defect between the pharynx and remaining intrathoracic stomach. One patient undergoing colonic interposition required removal of the graft after 4 days because of venous infarction. A gastric interposition graft was used successfully to restore alimentary continuity. Two of the three cervical chyle fistulas were treated by reexploration of the neck wound and ligation of the injured thoracic duct; the other resolved with a cervical pressure dressing and wound suction. In 2 of the 3 patients who experienced cerebrovascular accidents, the complication was transient and followed deliberate ligation and resection of a common carotid artery.

The morbidity associated with isolated anterior mediastinal tracheostomy was substantially less. Complications in this group of 10 patients included partial skin-flap necrosis (2), hypoparathyroidism (1), and esophageal leak (1). Six patients had an uncomplicated postoperative course. The duration of hospitalization ranged from 12 to 57 days (average time, 20.4 days), and 6 patients (60%) were discharged from the hospital within 14 days after operation.

Six of the 9 patients with hypoparathyroidism and hypothyroidism require long-term calcium and vitamin D therapy as well as thyroid hormone replacement. All 3 patients in whom the resected parathyroid glands could be identified and reimplanted in the pectoralis major muscle were normocalcemic without supplemental calcium within 6 months of operation.

Functional Results

In all surviving patients, a satisfactory airway was achieved and maintained with anterior mediastinal tracheostomy. Stenosis of the tracheostome in 8 patients has been managed by insertion of a Silastic (Dow Corning) Helsper stoma vent (Heyer-Schulte Company), which the patients frequently use only while asleep at night. The ability to maintain adequate nutrition by means of oral feedings has been achieved in all patients. After a pharyngogastric anastomosis, postprandial regurgitation during coughing, bending, or assuming the supine position is a common problem. However, within several months after operation, patients uniformly learn to limit the amount of food they eat at one time and to remain upright for at least 1 to 2 hours after eating so that the intrathoracic stomach can empty, and late complaints about regurgitation beyond 6 months are very unusual. Five patients have reported varying degrees of postprandial diarrhea or cramping (postvagotomy dumping syndrome) that generally responds to dietary measures (avoiding overdistention of the stomach and a high carbohydrate intake) and antispasmodics (eg, diphenoxylate hydrochloride and Kaopectate [Upjohn Co, Kalamazoo, MI]).

Survival

Survival after anterior mediastinal tracheostomy is related to the underlying disease process. Of the 4 patients who underwent anterior mediastinal tracheostomy for benign stomal stenosis after prior laryngectomy, 3 were lost to follow-up after 20 months, 24 months, and 44 months, and 1 is alive and well after 36 months. This patient, who had an anterior mediastinal tracheostomy for stomal stenosis associated with osteoradionecrosis of the sternum, had innominate vein erosion 7 months later. At reoperation, the innominate vein was ligated and divided, and the tracheal stump was transposed beneath the innominate artery. She has done well for the past 29 months. Of the other 6 patients undergoing isolated anterior mediastinal tracheostomy for recurrent laryngeal carcinoma, 4 died of metastatic disease after 8 months, 8 months, 9 months, and 19 months, and 2 are alive and without evidence of tumor 3 years and 10 years after operation.

The 2 patients undergoing combined anterior mediastinal tracheostomy and cervical exenteration for thyroid cancer died of metastatic disease after 18 and 48 months. The patient with a high malignant tracheoesophageal fistula died of metastatic disease after 3 months. Of the 5 patients with locally advanced laryngeal carcinoma, 3 died of locally recurrent tumor and distant metastasis after only 2, 6, and 12 months, and 2 are alive and well after 6 and 9 months of follow-up. Of the 4 of 6 patients surviving resection of pharyngeal or hypopharyngeal carcinomas, 3 died of metastatic disease after 2 months, 7 months, and 10 months, and 1 alcoholic patient who continued his habit postoperatively died of aspiration into the tracheostome while inebriated 6 months after operation. Sixteen of the 20 patients with postcricoid or cervicothoracic esophageal malignancies survived the operation. Nine died within 12 months (1 of a cerebrovascular accident, 1 of aspiration into the tracheostome while inebriated, and 7 of metastatic disease); 2 died of metastatic disease 13 and 24 months after operation; 1 died of metastasis after 28 months; and 1 died of progressive cancer after 41 months. Three are alive: 2 have metastatic disease after 12 and 41 months, and 1 is disease free after 69 months. The average survival of these 16 patients was 24 months.

Comment

In the 1940s and 1950s, several anecdotal reports were published describing attempts to establish a satisfactory airway in the intrathoracic trachea [5–9]. In 1962, Sisson and associates [10] reported that they removed the clavicles and manubrium to gain access to the thoracic trachea in 6 patients with stomal recurrences and rotated skin and pectoralis muscle flaps to construct an anterior mediastinal tracheostomy. Since then, Sisson and co-workers [11, 12] have published one of the most extensive experiences with anterior mediastinal tracheostomy for laryngotracheal and cervical esophageal carcinomas.

In 1966, Grillo [2] first described use of a bipedicled upper thoracic apron flap with resection of the anterior thoracic breastplate for construction of an anterior mediastinal tracheostomy in 3 patients with thyroid and laryngeal carcinoma. This technique was subsequently modified by Stell and associates [13], who used a wider bipedicled upper thoracic apron flap and resected half of the manubrium, medial clavicles, and first rib on only one side. Grillo [14] emphasized that anterior mediastinal tracheostomy has very limited application and that superior mediastinal hematoma, infection, and innominate artery rupture were major complications associated with this procedure. He [15] later described prophylactic division of the innominate artery to prevent late innominate artery erosion and protection of the great vessels of the superior mediastinum with an omental pedicle.

In our 1979 report of 17 anterior mediastinal tracheostomies, Dr Sloan and I [1] used Grillo's bipedicled upper thoracic apron flap in 13 patients but also emphasized the value of the thoracoacromial nipple flap described by Conley [16] and Sisson [17] to resurface the anterior neck and mediastinum in cases requiring dissection of cervical skin involved by tumor, a procedure we used in 4 patients. We transposed the tracheal stump beneath the innominate artery, as originally described by Waddell and Cannon [9], in 5 (29%) of our 17 patients to minimize tension between the trachea and skin and resulting pressure against the innominate artery. In patients requiring concomitant cervical exenteration, transhiatal esophagectomy without thoracotomy and a pharyngogastric anastomosis when possible was advocated.

In the past decade, the ideal method of reestablishing alimentary continuity after laryngopharyngectomy has been debated and has included myocutaneous flaps, free jejunal grafts, stomach, and colon [18–24]. Reporting the Massachusetts General Hospital experience, Grillo and Mathisen [25] recently described their series of 18 patients undergoing cervical exenteration, including 14 patients who required mediastinal tracheostomy. Emphasizing concern about the possibility of innominate artery erosion postoperatively, they advocate prophylactic division of the innominate artery after preoperative aortic arch angiography and intraoperative electroencephalographic monitoring after clamping the vessel for 10 minutes before dividing it. They divided the artery in 7 of their 14 patients undergoing anterior mediastinal tracheostomy. Expanding on their use of omental pedicles in complicated cardiothoracic problems [26], they advise interposing omentum between the mediastinal great vessels, the trachea, and the skin, a procedure they view as critical "in eliminating problems of erosion of the great vessels."

With greater experience with the technique of mediastinal tracheostomy, I have found that it is unnecessary to construct the "visor" or bipedicled apron flap advocated by Grillo and Mathisen. Vigorous retraction of the anterior thoracic skin through an extended supraclavicular collar incision permits resection of the anterior thoracic breastplate and construction of the mediastinal tracheostomy in better-vascularized upper thoracic skin, frequently within the line of closure of the skin. At The University of Michigan Medical Center, we have not used the bipedicled apron flap in our last 23 anterior mediastinal tracheostomies.

It is increasingly apparent that the most critical step in constructing an anterior mediastinal tracheostomy is assessing the degree of tension between the remaining tracheal stump, the anterior thoracic skin, and the adjacent innominate artery. Because the innominate artery and the trachea are normally in apposition, there is absolutely no reason that erosion of the vessel by the trachea should occur *unless* undue tension of one against the other is created in the process of constructing the tracheostomy. If there is the *slightest* concern that tension between these two structures is occurring, transposition of the divided trachea beneath and to the right of the innominate artery should be carried out. There simply cannot be pressure necrosis of the trachea against the innominate artery if the trachea is angled forward to reach the skin *beneath* the artery.

In our 44 mediastinal tracheostomies, we experienced one innominate artery erosion early in our experience before we lowered our threshold for tracheal transposition, a technique we have used in nearly one third of all of our patients and in eight of our last 15 mediastinal tracheostomies. We have not divided the innominate artery in *any* of our patients, nor have we interposed omentum or muscle flap between the artery and trachea. On the basis of our experience, it is concluded that innominate artery erosion should rarely, if ever, complicate anterior mediastinal tracheostomy if proper attention to detail is paid and tension on the vessel is strictly avoided.

When cervical exenteration is required, the method of reestablishing alimentary continuity remains controversial. I prefer the addition of a transhiatal esophagectomy and use of the stomach brought through the posterior mediastinum in the original esophageal bed for a pharyngogastric anastomosis. The simplicity of a single pharyngeal anastomosis has obvious appeal compared with the multiple intraabdominal anastomoses required for colonic interposition or the intestinal and microvascular anastomoses of jejunal interposition. There is little doubt, however, that maximum cephalad reach of the stomach is required for construction of a pharyngogastric anastomosis. Relative tension on the anastomosis unquestionably accounts for the 29% leak rate we have experienced with our pharyngogastric anastomoses, more than three times the leak rate we have had with standard cervical esophagogastric anastomoses after routine transhiatal esophagectomy. The impact of prior radiation therapy on impaired healing in these patients may also be a contributing factor. These anastomotic leaks, however, have generally been quite innocuous and well managed with Jackson-Pratt wound drains, which are routinely placed on either side of the anastomosis intraoperatively and left undisturbed until a postoperative barium swallow on the tenth postoperative day ensures healing of the anastomosis. I accept the relative increased risk of a pharyngogastric anastomotic leak rather than the increased operative time, complexity, and potential postoperative complication rate of colonic interposition or other methods of esophageal reconstruction. Greater use of anastomotic buttressing with an omental pedicle left attached to the high greater curvature may reduce our leak rate in the future.

Anterior mediastinal tracheostomy clearly facilitates resection of cervicothoracic tracheal and esophageal malignancies, and of the 47 cervical exenterations we have performed, 34 (72%) were associated with concomitant mediastinal tracheostomy, similar to the 77% rate of mediastinal tracheostomy with cervical exenteration reported by Grillo and Mathisen [25]. Anterior mediastinal tracheostomy combined with cervical exenteration, transhiatal esophagectomy, and one-stage pharyngogastric anastomosis is a formidable technical exercise, the justification for which can be questioned when long-term survival of patients with cervicothoracic esophageal and tracheal malignancies is not often achieved. This approach, however, provides efficient palliation and occasional cure in these patients whose airway, swallowing ability, or both are often gravely compromised, and excellent results with an acceptable morbidity can be achieved with careful patient selection, meticulous attention to operative detail, and intensive postoperative care.

References

1. Orringer MB, Sloan H. Anterior mediastinal tracheostomy. Indications, techniques, and clinical experience. J Thorac Cardiovasc Surg 1979;78:850–9.
2. Grillo HC. Terminal or mural tracheostomy in the anterior mediastinum. J Thorac Cardiovasc Surg 1966;51:422–7.
3. Orringer MB, Sloan H. Esophagectomy without thoracotomy. J Thorac Cardiovasc Surg 1978;76:643–54.
4. Orringer MB. Technical aids in performing transhiatal esophagectomy without thoracotomy. Ann Thorac Surg 1984;38: 128–32.
5. Watson WL. Cancer of trachea fifteen years after treatment for cancer of larynx. J Thorac Surg 1942;12:142–50.
6. Sloan H, Cowley RA. Posterior mediastinal tracheostomy. J Thorac Surg 1951;21:602–7.
7. Kleitsch WP. Anterior mediastinal tracheostomy. J Thorac Surg 1952;24:38–42.
8. Minor GR. Trans-sternal tracheal excision for carcinoma. J Thorac Surg 1952;24:88–92.
9. Waddell WR, Cannon B. A technique for subtotal excision of the trachea and establishment of a sternal tracheostomy. Ann Surg 1959;149:1–8.
10. Sisson GA, Straehley CJ Jr, Johnson NE. Mediastinal dissec-

tion for recurrent cancer after laryngectomy. Laryngoscope 1962;72:1064–77.
11. Sisson GA, Edison BD, Bytell DE. Trans-sternal radical neck dissection, postoperative complications and management. Arch Otolaryngol 1975;101:46–9.
12. Sisson GA, Bytell DE, Becker SP. Mediastinal dissection—1976: indications and newer techniques. Laryngoscope 1977; 87:751–9.
13. Stell PM, Bickford BJ, Brown GA. Thoracotracheostomy after resection of the larynx and cervical trachea for cancer. J Laryngol Otol 1970;84:1097–1102.
14. Grillo HC. Surgery of the trachea. Curr Probl Surg 1970:3–59.
15. Grillo HC. Discussion of Orringer and Sloan [1].
16. Conley JJ. The use of regional flaps in head and neck surgery. Ann Otol Rhinol Laryngol 1960;69:1223–34.
17. Sisson GA. Flaps and grafts in head and neck surgery. Minn Med 1967;50:952–60.
18. Frederickson JM, Wagenfeld DJH, Pearson G. Gastric pull-up vs. deltopectoral flap for reconstruction of the cervical esophagus. Arch Otolaryngol 1981;107:613–6.
19. Withers EH, Davis JL, Lynch JB. Anterior mediastinal tracheostomy with a pectoralis major musculocutaneous flap. Plast Reconstr Surg 1981;67:381–4.
20. Spiro RH, Shah JP, Strong BW, Gerold RP, Bains MS. Gastric transposition in head and neck surgery: indications, complications, and expectations. Am J Surg 1983;146:483–7.
21. Moores DWO, Ilves R, Cooper JD, Todd TRJ, Pearson FG. One-stage reconstruction for pharyngolaryngectomy: esophagectomy and pharyngogastrostomy without thoracotomy. J Thorac Cardiovasc Surg 1983;85:330–6.
22. Goldberg M, Freeman J, Gullane PJ, et al. Transhiatal esophagectomy with gastric transposition for pharyngolaryngeal malignant disease. J Thorac Cardiovasc Surg 1989;97:327–33.
23. Gomes MN, Kroll S, Spear SL. Mediastinal tracheostomy. Ann Thorac Surg 1987;43:539–43.
24. Paletta CE, Jurkiewicz MJ. Esophageal replacement: microvascular jejunal transplantation. In: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS, eds. Glenn's thoracic and cardiovascular surgery. 5th ed. Norwalk, CT: Appleton and Lange, 1991:819–26.
25. Grillo HC, Mathisen DJ. Cervical exenteration. Ann Thorac Surg 1990;49:401–9.
26. Mathisen DJ, Grillo HC, Vlahakes GJ, Daggett WM. The omentum in the management of complicated cardiothoracic problems. J Thorac Cardiovasc Surg 1988;95:677–84.

DISCUSSION

DR DOUGLAS J. MATHISEN (Boston, MA): I congratulate Dr Orringer on his usual outstanding presentation and thank him for the privilege of reviewing the manuscript before the meeting this morning.

This is an important contribution to a very, very difficult problem. Anybody in the audience who has dealt with such patients understands the amount of work that goes into caring for them. The operations are very demanding and require meticulous attention to detail and dedicated postoperative care to get a good result. Dr Orringer's contribution is most remarkable in its results and the body of work that it encompasses. I am certain that in the new relative value scale, this probably will have a value at least equivalent to a tracheostomy when they get done assigning relative values to it.

Our experience has been detailed in the past, and I will not go into that except to say that it is really remarkably similar to that of Dr Orringer and that the differences in approach are really quite subtle. However, these differences do beg a couple of questions.

My colleagues and I certainly agree that the routine use of division of the innominate artery is not necessary. In our experience, the patients in whom we have divided this artery have been patients in whom the distal tracheal segment has been less than 4 cm. In your experience, how many of your patients had a distal tracheal segment of less than 4 cm? With this amount of distal trachea, is it more difficult to transpose it, as you suggest? The second point about transposing the trachea is whether or not it adds anything to the ischemia of the trachea, especially in an irradiated trachea, and whether you think there is an element of posterior pressure when it is transposed in front of the innominate artery.

We think the omentum is an important adjunct to this procedure for a couple of reasons. As in your series, many of our patients have had high-dose irradiation to the cervical area from prior malignancies. We have used the omentum as an adjunct to healing and think that it contributes to a lower leak rate with an anastomosis between either stomach or colon and an irradiated pharynx. Another reason for using the omentum is as a protective device for the great vessels in case there is retraction of the stoma. What are your thoughts about the role the omentum might play to aid in healing and possibly reduce the leak rate that you have seen in your series?

You also alluded to the contribution of tension in some of the problems that you have seen. Certainly every time I have done a transhiatal esophagectomy and tried to get the stomach to the hypopharynx, there is the problem of not having it reach quite as well as I would like. Would you share with us any important tricks you use to give some extra length to the stomach when you are going virtually to the base of the tongue? Would not the anterior route provide a more easily accessible pathway for the stomach as opposed to the more conventional approach in the posterior mediastinum?

DR ORRINGER: Thank you, Dr Mathisen. As usual, there is a great deal of insight into this report from an individual who is actually doing this work. As I mentioned, a 5-cm minimal length of remaining trachea is optimal for construction of an anterior mediastinal tracheostomy. With less than that, one is starting to test the boundaries of what is feasible. In most of these patients, the remaining trachea is quite short, and it is possible to look in and see the carina within a few centimeters of the skin. I would say that very few of our patients, perhaps not more than 4 or 5, have had a remaining tracheal length of less than 4 cm. I do not believe that mobilizing the remaining trachea below and to the right of the innominate artery increases ischemia if in so doing, one follows the dictum Dr Grillo established years ago that mobilization of the trachea should be done only in front and in back of the trachea, never laterally, so as not to disturb the blood supply. I believe that avoiding skeletonizing the innominate artery (leaving the adventitia in place) and transposing the tracheal stump beneath the artery absolutely eliminate any possibility of subsequent tension and erosion.

The contribution of the group at Massachusetts General Hospital in using the omental flap both as an adjunct to healing and as a protective cover over the great vessels is extremely important and worth heeding. Again, I am less concerned with protecting the vessels from erosion by the adjacent trachea. In every one of us, the innominate artery is normally opposing the trachea, and the reason it does not erode is that there is no tension between these two structures. In constructing an anterior mediastinal tracheostomy, if the tracheal stump is transposed inferiorly when there is any concern about tension between these two organs, there simply will not be later erosion.

Certainly construction of a pharyngogastric anastomosis requires the highest reach the stomach must make. It is important, therefore, to elongate the stomach as the lesser curvature is progressively divided with the GIA stapler, stretching the stomach with each application of the stapler to gain maximum reach. After the stomach is anastomosed to the pharynx, we leave Jackson-Pratt drains on either side of the anastomosis for 10 days until the postoperative barium swallow is completed. A high pharyngogastric anastomotic leak often responds to local, simple drainage through the drains that are already in place. We have had only one stomach that has separated to the point that we have had to use a jejunal interposition to bridge the remaining gap. If one measures the distance from the neck to the abdominal cavity, the shortest route is through the posterior mediastinum, next the retrosternal route, and then, the longest, the anterior thoracic route in front of the sternum. The posterior mediastinal route for esophageal replacement in these patients is preferable for another important reason, and that is that after 72 hours, the stomach is adherent to the prevertebral fascia in most patients, and the mediastinum is effectively closed off from the neck wound.

In closing, I will make one other technical point, with an illustrative case report. One of our patients had a tracheal stomal recurrence after laryngectomy and underwent a tracheal stomal resection, anterior mediastinal tracheostomy, and thoracoacromial nipple flap rotation from the left, with skin grafting of the remaining defect. The nipple was mobilized upward, hence the name nipple flap. Ten years later, the patient had resection of the nipple under local anesthesia for cosmetic reasons.

For patients in whom a stomal stenosis develops after mediastinal tracheostomy, there is the Helsper stoma vent, a silicone rubber prosthesis that comes in various sizes and is quite easy for the patient to insert and remove as necessary. This provides an easy way to treat any subsequent stomal stenosis after mediastinal tracheostomy. This vent is made by the Heyer-Schulte Company, which makes the Angelchik prosthesis (one of the better investments of the company).

Postpneumonectomy Syndrome: Diagnosis, Management, and Results

Hermes C. Grillo, MD, Jo-Anne O. Shepard, MD, Douglas J. Mathisen, MD, and David J. Kanarek, MD

General Thoracic Surgical Unit, Department of Radiology, and Pulmonary Unit of the Department of Medicine, Massachusetts General Hospital, and Departments of Surgery, Radiology, and Medicine, Harvard Medical School, Boston, Massachusetts

Airway obstruction may be caused by extreme mediastinal shift and rotation after right pneumonectomy or after left pneumonectomy in the presence of a right aortic arch. Eleven adults (aged 18 to 58 years) with severe symptoms were treated surgically between 5 months to 17 years after pneumonectomy (7 right, 4 left). An initial patient with only one functional lobe was treated unsuccessfully by aortic division and bypass graft. Ten underwent mediastinal repositioning. After two recurrences prostheses were used to maintain mediastinal position. Five patients who underwent such repositioning are doing well from 5 months to more than 5 years later. One died 1 month after operation probably of pulmonary embolism. One who showed residual airway collapse after operation has some recurrent obstruction. Three other patients who showed severe malacic obstruction of the airway after mediastinal repositioning variously underwent aortic division with bypass graft and tracheal and bronchial resection. One is well almost 6 years later. Two died postoperatively. Occurrence of the syndrome is unpredictable. Where malacic changes have not occurred, mediastinal repositioning may reasonably be expected to correct obstruction. Optimal treatment for concurrent severely malacic airways is unclear.

(Ann Thorac Surg 1992;54:638–51)

Severely symptomatic airway compression may be caused by extreme mediastinal shift and rotation after right pneumonectomy. Herniation of the lung with overdistention accompanies this. The problem has been particularly noted in children, but it also occurs in adults throughout a wide age span [1–8]. Similar airway compression may follow left pneumonectomy in the presence of a right aortic arch [5, 9]. We report experiences in the diagnosis and management of 11 adults with severe symptoms from these problems. The patients fall into two groups, one in which mechanical compression alone is present and the second in which secondary malacia of the airway cartilages has occurred.

Material and Methods

Eleven patients were evaluated and treated surgically between 1979 and 1991 for severe manifestations of postpneumonectomy syndrome. The syndrome followed right pneumonectomy in 7 patients and left pneumonectomy in the presence of a right aortic arch in 4 patients. Records were reviewed in detail. Because patients came from a wide geographic spread, follow-up was necessarily carried out for the most part by patient questionnaire and with the cooperation of referring physicians. Preoperative and postoperative pulmonary function studies were compared. Postoperative values were obtained at intervals from just before discharge after operation to 6 years later.

Bronchoscopic examinations were primarily performed with a flexible bronchoscope under topical anesthesia in order best to study dynamic changes with respiration and cough.

Preoperative and postoperative radiographic and other imaging studies were reviewed retrospectively. Preoperative studies included serial chest radiographs in the posteroanterior and lateral projections in all cases. Computed tomography (CT) of the chest was performed in all 11 patients, in 2 of whom it included inspiratory and expiratory images of the airways. Computed tomographic scans were obtained on fourth-generation General Electric or Technicare scanners. Contiguous 10-mm scans were obtained through the lungs, and 5-mm scans were obtained through the hilar regions. Intravenous contrast enhancement of mediastinal vessels was employed using a bolus technique. Magnetic resonance imaging of the mediastinum and hilar regions was performed in 4 of the more recent patients. Scans were obtained on Teslecon (0.6 T) or GE (1.5 T) scanners. T1-weighted images were obtained in the sagittal, coronal, and axial planes. Respiratory compensation and cardiac gating were employed. Conventional tomography of the trachea and bronchi was performed in 2 patients in the anteroposterior and lateral projections. The technique included 0.5-cm slice thicknesses and a 20-degree arc. Chest fluoroscopy of the airways was performed in 7 of the 11 patients to evaluate for the presence of tracheobronchomalacia. Postoperative imaging included serial anteroposterior portable chest radiographs and posteroanterior and lateral chest radiographs before discharge from the hospital. Postoperative CT of the chest was performed in 8 patients. Conventional

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Grillo, Massachusetts General Hospital, Boston, MA 02114.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

tomography of the mediastinum was performed in 1 patient in lieu of CT. Postoperative chest magnetic resonance imaging was performed in 1 patient.

Clinical Observations and Anatomic Definition

PATIENT POPULATION AND SYMPTOMS. Seven of the 11 patients were female (Table 1). The age at the time of attempted corrective operation ranged between 18 and 58 years. Four patients were in the second decade, 3 in the third, 1 in the fifth, and 3 in the sixth. Intervals between the original pneumonectomy and the time of attempted correction ranged from 5 months to 17 years. Two patients had undergone pneumonectomy in childhood. One of these had pneumonectomy for pulmonary tuberculosis and the other for complications of congenital hypoplastic lung. Four of the adult patients underwent pneumonectomy for complications of congenital lung disease between 5 months and 3⅔ years before corrective operation. Of the remaining 5 patients, 4 had undergone pneumonectomy for neoplastic disease and 1 for trauma, which included avulsion of the right main bronchus and laceration of the trachea.

The 4 patients who had difficulty after left pneumonectomy, all of whom had right aortic arch, suffered from complications of congenitally hypoplastic left lung with hypoplastic pulmonary artery. The indication for pneumonectomy had been hemorrhage in 3 of these and chronic infection in 1.

All patients had progressive and incapacitating dyspnea that occurred on minimal effort and in the most severely affected patients was present at rest. Audible stridor was noted in 6. Recurrent infection was present in 4. One suffered near respiratory arrest.

PULMONARY FUNCTION STUDIES. Pulmonary function studies (Tables 2, 3) evidenced upper airway obstruction. Forced vital capacity (FVC) was in many cases greater than expected in a patient who had undergone pneumonectomy, reflecting overexpansion of the residual lung. Although the forced expiratory volume in 1 second (FEV_1) varied and was not always strikingly altered from what might be expected in a pneumonectomy patient, the FEV_1/FVC ratio was generally much reduced. Peak flow was markedly diminished, and the residual volume/total lung capacity ratio was increased.

PREOPERATIVE IMAGING STUDIES. In the chest radiographs of the 7 patients after right pneumonectomy, the trachea projected to the right of the spine and the left main bronchus was seen crossing from right to left anterior to the spine. The heart and great vessels were shifted into the right hemithorax against the right posterolateral chest wall (Fig 1). The left lung was hyperinflated and clear in all patients except patient 1 in whom bronchiectasis, mucous plugging, and fibrosis had developed in the left lower lobe. In the 4 patients after left pneumonectomy, the trachea was markedly shifted to the left of the spine. The right main and lobar bronchi coursed from left to right anterior to the spine, and the heart and great vessels assumed a position against the left posterolateral chest wall. The right lung was markedly hyperinflated and herniated into the left hemithorax (Fig 2). Scoliosis was present in all 11 patients.

Sequential chest radiographs from the time of pneumonectomy to admission for operative repair were available for review in 3 patients. These demonstrated gradual shift of the mediastinum from its prepneumonectomy position to a markedly abnormal position against the chest wall in periods between 5 and 13 months. Mediastinal shift coincided with the onset of symptoms in each patient.

Postpneumonectomy computed tomographic studies confirmed the plain radiographic findings and contributed additional information regarding the postpneumonectomy space, the relative position of the mediastinal vessels, bronchi, and thoracic spine, and the specific site of bronchial obstruction (Figs 3, 4). After right pneumonectomy the mediastinum shifted posterolaterally to the right and rotated about 90 degrees in a counterclockwise direction (relative to the spine, from the standard computed tomographic perspective looking cephalad from the feet) such that the aortic arch and left pulmonary artery assumed a horizontal position. In all 7 patients the left main bronchus (LMB) was markedly narrowed as it coursed posterior to the left pulmonary artery (see Fig 3). In 5 of the 7 patients the LMB was interposed between the left pulmonary artery anteriorly and the descending aorta and spine directly posteriorly (Fig 5). In the other 2 patients the LMB was interposed between the left pulmonary artery and the thoracic spine. In these 2 patients the descending aorta was to the left of the spine (patients 5 and 8) separate from the bronchus. In neither of these 2 patients was malacia present. A left aortic arch was noted in all 7 patients.

After left pneumonectomy the heart and great vessels shifted to the left posteriorly and laterally against the chest wall and rotated clockwise about 90 degrees relative to the spine. A right-sided aortic arch was present in all 4 patients. The right main, right upper, and right lower lobe bronchi were splayed anterior to the aorta and spine and markedly narrowed (see Fig 4). Inspiratory and expiratory images of the bronchi showed further narrowing on expiration in 1 of 2 patients.

In all 11 patients, the postpneumonectomy space was very small or nonexistent.

Magnetic resonance imaging performed in 4 patients confirmed the findings seen on CT. However, due to the respiratory motion and subsequent decreased spatial resolution the smaller lobar and segmental bronchi were not well imaged on magnetic resonance imaging. In 3 patients the right-sided aortic arch was well demonstrated in the coronal plane (Fig 6). A cine sequence was obtained in 1 patient (patient 10) demonstrating the pulsatile effects of the posteriorly located aorta on the right-sided bronchi (Fig 7).

Preoperative fluoroscopy was performed in 7 patients. In 3 patients who were proved to have malacia, fluoroscopy correctly identified the malacic segment preoperatively. However, in 4 other patients abnormal collapse

Table 1. Postpneumonectomy Syndrome: Surgical Management

Patient No.	Age at Time of Correction (y)	Sex	Original Disease	Pneumonectomy (date and side)	Corrective Procedures	Interval Between Original & Corrective Operations	Early Result	Length of Follow-up	Late Result
1	19	F	Pulm tbc, bronchiectasis	'62 RUL '65 RML, RLL	2/79 LL lobect, aortic division and bypass 2/79 LM bronchial resection	17 y	Died postop of pneumonia, bronchomalacia, fibrosing alveolitis	. . .	. . .
2	18	M	Trauma: avulsion RMB, trach lac	9/83 R and trach repair	2/85 Reposition (no prosthesis) 2/85 long T tube 5/85 Reposition, T tube 7/85 LMB resection, aortic division and bypass 8/85 Trach-bronch resection: cerv trachea divided 1/86 Tracheal reconstruction	1 y 5 mo	Reposition without prosthesis failed, persistent airway malacia; reoperations required	5 y 11 mo	Good; hoarse
3	56	F	Adenoca	12/78 R	5/85 Reposition (no prosthesis) 11/86 Repositon (800 mL)	6 y 6 mo	Initial reposition without prosthesis failed; reoperated	5 y 11 mo	Good
4[a]	19	F	Hypoplastic L lung; R aortic arch, pectus excavatum	5/85 L	3/86 Reposition (750 mL)	10 mo	Good	5 y 8 mo	Good
5	19	F	Cong cystic lungs with hemorrhage	8/85 R	9/86 Reposition (800 mL)	1 y 1 mo	Good (Dressler's syndrome at 8 mo)	4 y 7 mo	Good *re* pulm; leiomyosarcoma, stomach 12/87
6[a]	26	F	Hypoplastic lung, R aortic arch	'66 L	12/86 Reposition (no prosthesis), carinal resection, vertebral resection 12/86 Aortic bypass 2/86 Pericardiotomy 1/87 Trach-bronch resection, aortic division	20 y	Pericardial tamponade after aortic graft, relieved; died postop of resp failure, viscid casts in bronchial tree	. . .	. . .
7	41	F	Carcinoid RMB	'85 R, radiotherapy	5/88 Reposition (750 mL)	2 y	Improved, some residual collapse of bronchi	3 y 7 mo	Progressive narrowing LMB, dyspnea
8	55	M	Squamous ca	'81 R	8/88 Reposition (900 mL)	7 y	Good, initially	1 mo	Bronchospasm 1 mo postop; responded; airway patent and stable; sudden death, clinical diagnosis: pulmonary embolism (no autopsy)
9	55	M	Ca lung	'80 R	8/88 Reposition (900 mL), T tube 8/88 Aortic division & bypass	8 y	Died postop of resp failure, bronchomalacia, bronchopneumonia, pulmonary emboli	. . .	. . .
10[a]	24	M	Hypoplastic lung, hemorrhage, R aortic arch	2/91 L	7/91 Reposition (1,130 mL)	5 mo	Pericardial compression, mild, <1 wk, then good	7 mo	Good
11[a]	29	F	Hypoplastic lung, hemorrhage, R aortic arch	5/90 L	9/91 Reposition (1,260 mL)	1 y 4 mo	Good	5 mo	Good

[a] Right aortic arch present.

Adenoca = adenocarcinoma; ca = carcinoma; cong = congenital; L = left; lac = laceration; LL = left lower; LM = left main; LMB = left main bronchus; lobect = lobectomy; pulm = pulmonary; R = right; resp = respiratory; RLL = right lower lobe; RMB = right main bronchus; RML = right middle lobe; RUL = right upper lobe; tbc = tuberculosis; trach = tracheal; trach-bronch = tracheobronchial.

Table 2. Preoperative and Postoperative Spirometry

	Preoperative Testing (% predicted)					Postoperative Testing (% predicted)				
Patient No.	Date	FEV_1 (L)	FVC (L)	FEV_1/FVC	PEFR (L/s)	Date	FEV_1	FVC	FEV_1/FVC	PEFR
3	1/14/85	1.48 (60%)	2.54 (77%)	0.58 (70%)	2.21 (37%)	9/18/91	1.31 (53%)	1.68 (53%)	0.78 (101%)	3.1 (52%)
4	3/13/86	1.07 (29%)	1.66 (39%)	0.64 (73%)	1.97 (29%)	5/16/88	1.17 (35%)	1.52 (39%)	0.77 (80%)	2.5 (36%)
5	9/25/86	0.35 (9%)	1.78 (40%)	0.19 (22%)	0.48 (7%)	11/18/86	1.85 (47%)	2.17 (47%)	0.85 (101%)	3.37 (46%)
7	5/16/88	1.72 (61%)	2.44 (72%)	0.71 (87%)	2.31 (40%)	9/30/88	1.35 (52%)	1.78 (56%)	0.76 (93%)	2.63 (51%)
8	8/1/88	0.81 (20%)	1.57 (31%)	0.52 (67%)	1.89 (20%)	8/10/88	1.15 (28%)	1.77 (34%)	0.65 (83%)	3.67 (39%)
10	7/15/91	1.23 (26%)	3.08 (54%)	0.4 (48%)	2.88 (29%)	7/31/91	1.66 (35%)	2.66 (47%)	0.63 (76%)	4.5 (45%)
11	9/3/91	1.67 (52%)	2.83 (75%)	0.59 (69%)	3.1 (48%)	9/10/91	1.41 (43%)	1.73 (46%)	0.81 (94%)	3.91 (61%)
Mean ± SE		1.19 ± 0.19	2.27 ± 0.23	0.52 ± 0.07	2.12 ± 0.32		1.41 ± 0.10[a]	1.90 ± 0.15[a]	0.75 ± 0.03[b]	3.38 ± 0.27[b]

[a] Not significantly different from preoperative value. [b] $p < 0.05$ versus preoperative value.

FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEFR = peak expiratory flow rate; SE = standard error.

was identified fluoroscopically that did not persist after repositioning.

In all of the patients who underwent fluoroscopy after pneumonectomy, the bronchial narrowing in the LMB was seen best in the lateral projection where the narrowed LMB was demonstrated posterior to the left pulmonary artery and anterior to the spine or aorta and spine (see Fig 7). In the patients with a right-sided arch after left pneumonectomy, the precise location of right-sided bronchial obstruction was very difficult to identify by fluoroscopy.

Conventional tomography was performed in 2 of the earlier patients. Findings were similar to the plain radiographic findings. The site of LMB narrowing was identified only in the lateral projection.

Bronchoscopy showed displacement of the trachea to right or left, depending on the location of the aortic arch, and generally a marked lateral wall impression of the arch on the lower trachea, sometimes with a degree of compression of the lower trachea. The carina was rotated. The left main bronchus was compressed anteroposteriorly after right pneumonectomy, with variable increase in obstruction, often nearly complete, upon cough or deep expiration. The compression was pulsatile anteriorly and variable posteriorly and most marked in the proximal bronchus. The lobar bronchi were patent and appeared to be normal. After left pneumonectomy with right aortic arch, the right main bronchus was similarly compressed, but this effect extended into the upper lobe bronchus and the bronchus intermedius.

Surgical Management

Our surgical management has evolved in the course of treating these 11 patients. In our first patient (patient 1), who suffered from such extreme disability that she was unable to leave her bed, no attempt was made at repositioning the mediastinum. Effort was directed to relieving the compression on the left main bronchus by performing aortic division with bypass from the ascending aorta to the descending aorta. The left lower lobe in this patient proved to be fibrotic and could not be expanded even with forced ventilation intraoperatively. Lower lobectomy was therefore performed, leaving the patient with only the single functional lobe. Although direct compression of the bronchus as it was flattened against the aorta was relieved by aortic division, the airway was severely malacic and, therefore, left main bronchial resection was later performed to remove the flaccid segment. The patient could not be weaned from the ventilator postoperatively and died of pneumonia in the residual left upper lobe. Fibrosing alveolitis was also found at postmortem examination.

In the remaining 10 patients the mediastinum was repositioned in every case. The side of the original pneumonectomy was reopened and scar attachments lysed until the mediastinum including the heart and pericardium could be replaced in a central position and the

Table 3. Preoperative and Postoperative Plethysmography

	Preoperative Testing (% predicted)			Postoperative Testing (% predicted)		
Patient No.	TLC (L)	RV (L)	RV/TLC	TLC	RV	RV/TLC
7	3.5 (72%)	1.06 (64%)	0.3 (90%)	2.43 (51%)	0.63 (40%)	0.26 (76%)
8	7.55 (106%)	5.98 (241%)	0.79 (229%)	3.62 (49%)	1.85 (73%)	0.51 (148%)
10	5.69 (76%)	2.61 (141%)	0.46 (186%)	4.2 (56%)	1.54 (83%)	0.37 (150%)
11	7.36 (144%)	4.53 (290%)	0.62 (203%)	3.36 (66%)	1.63 (104%)	0.49 (161%)
Mean ± SE	6.03 ± 0.94	3.55 ± 1.08	0.54 ± 0.11	3.40 ± 0.37[a]	1.41 ± 0.27[b]	0.41 ± 0.06[b]

[a] $p < 0.05$ versus preoperative value. [b] Not significantly different from peoperative value.

RV = residual volume; SE = standard error; TLC = total lung capacity.

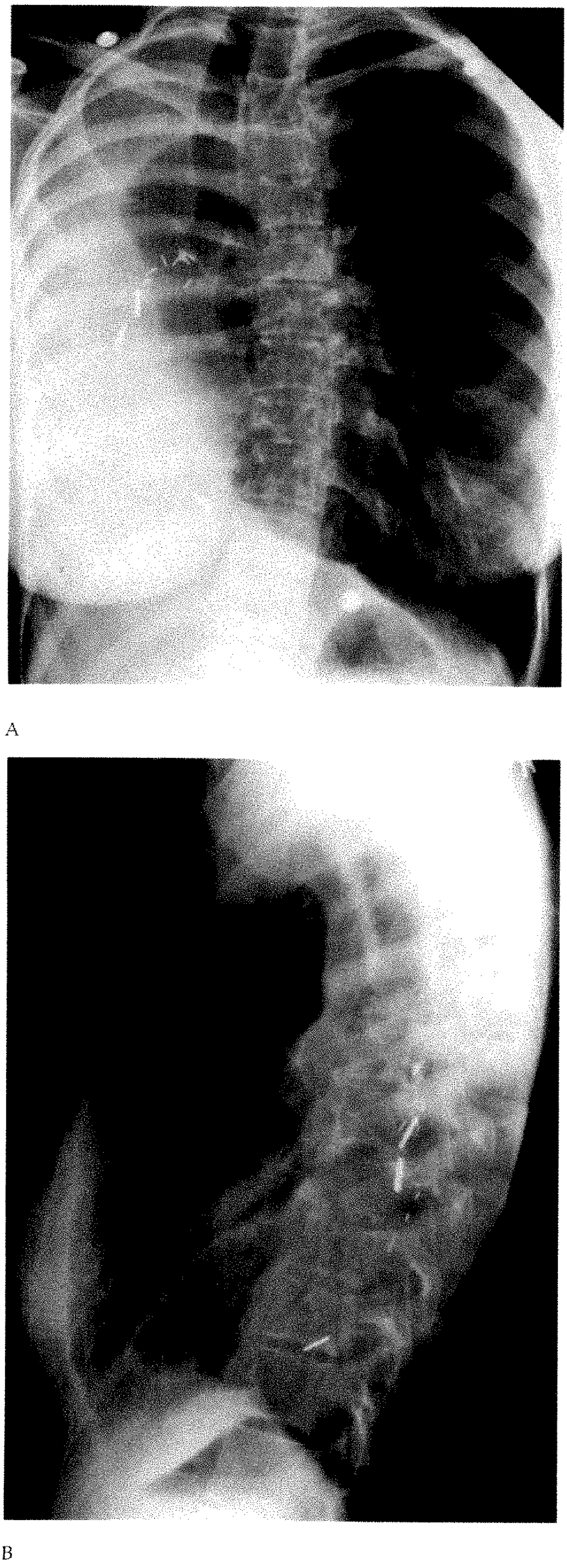


Fig 1. (Patient 5.) Eleven months after right pneumonectomy for congenital cystic lung with hemorrhage, posteroanterior (A) and lateral (B) chest films demonstrate marked shift of the trachea and mediastinum into the right hemithorax with the heart against the right posterolateral chest wall. There is herniation of the left lung into the right hemithorax.

herniated lung reduced to the opposite side. In the first 2 patients who underwent repositioning (see Table 1), the pericardium was sutured to the undersurface of the sternum with two vertical rows of 1-0 Prolene (Ethicon, Somerville, NJ) sutures. Care was taken to avoid reducing the volume of the pericardial sac excessively, observing for signs of tamponade as the sutures were placed. The pericardial surface was denuded and the posterior fascia overlying the back of the sternum abraded to attempt to obtain fusion for permanent fixation in this corrected position, without resort to foreign material as space filler. Any residual herniated lung in the upper mediastinum was reduced and the defect sutured. After repositioning the patients again underwent bronchoscopy with the flexible instrument intraoperatively; the endotracheal tube was withdrawn sufficiently to permit complete observation of tracheal and bronchial anatomy.

In the first of these patients (patient 2) severe residual malacia of the left main bronchus and lower trachea was observed. Although the interval had been only 17 months between the original pneumonectomy and this procedure, the patient had sustained a tracheal laceration with a linear repair performed originally. The collapsing airway was therefore stented with a long silicone T tube that extended beyond the softened area of the left main bronchus nearly to its bifurcation. The patient was discharged with the hope that the cartilages would stiffen up with time as usually occurs after removal of massive substernal goiters that have caused true malacia. This failed to happen. In addition, the mediastinum slipped back to some degree into the right chest. The patient therefore underwent a second repositioning and soon thereafter, when it was clear that the malacia had not been corrected by rigidification of the cartilages, a further operation was done to remove airway compression against the aorta. The aorta was divided after placement of a synthetic bypass graft, and the segment of malacic left main bronchus was resected. This also proved to be inadequate because of persistent distal tracheal malacia, and further resection of the distal trachea and origin of the left main bronchus was performed. This necessitated devolvement of the cervical trachea into the mediastinum with establishment of double stomas in the neck. These were finally reconstructed at a further procedure. The patient has remained well since, a span of nearly 6 years.

The third patient (patient 3), who underwent repositioning without prosthesis, also suffered recurrence of the syndrome as the mediastinum gradually moved back into the right chest. She underwent further repositioning 18 months later, this time with placement of an 800-mL

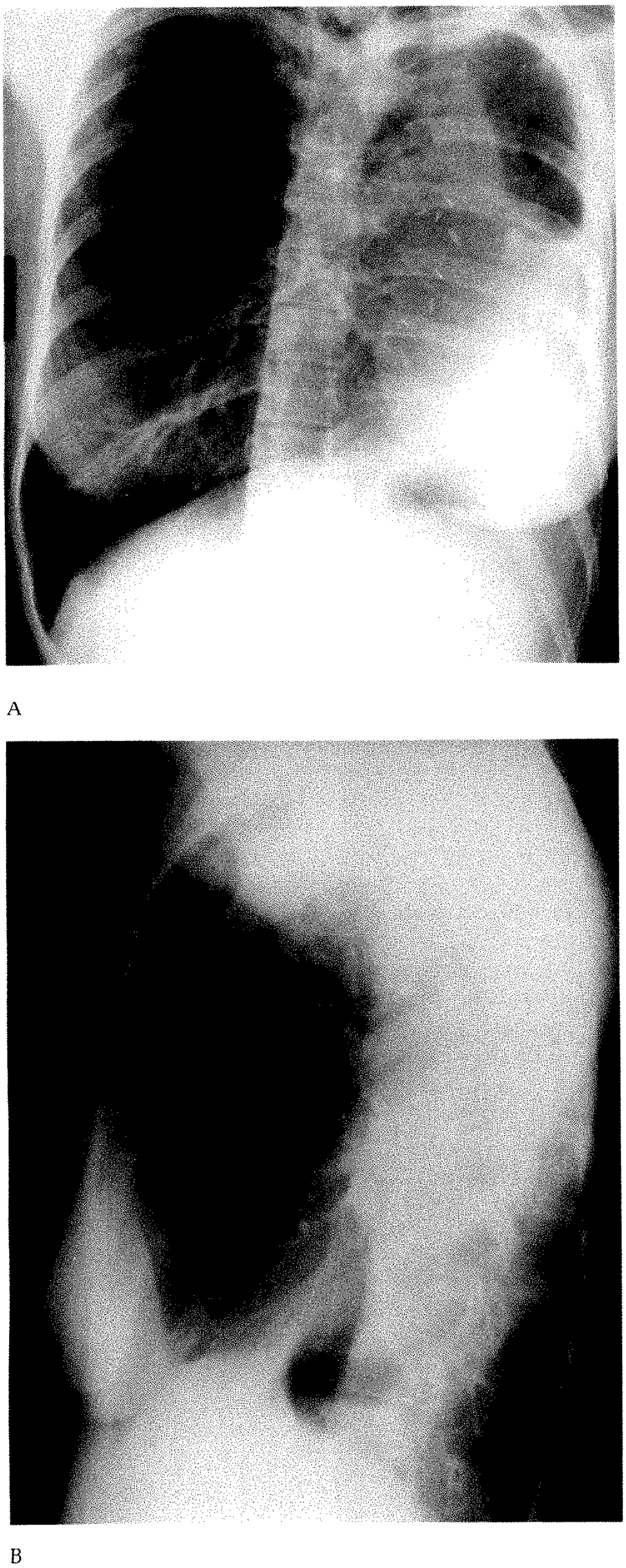


Fig 2. (Patient 11.) Sixteen months after left pneumonectomy for hypoplastic lung with hemorrhage, posteroanterior (A) and lateral (B) chest films demonstrate shift of the trachea and mediastinum into the left hemithorax with the heart against the posterolateral chest wall and herniation of the right lung into the left hemithorax.

silicone-filled breast prosthesis to fill the residual space in the right hemithorax to prevent recurrence. She remained well and fully active 4 years 10 months after this procedure.

In the balance of the patients, repositioning was accomplished either from the right side or the left side as described. It was elected in all of these patients to drop four intercostal muscles and attached periosteum into the chest to lie against the mediastinum, preserving the anterior and posterior attachments of the muscles. A strip of periosteum was preserved on the anterior surface of each rib for long-term maintenance of the bone. Filling prostheses were placed subcostally (except in patient 6) to lie against the mediastinum with the mobilized intercostal muscle bundles interposed between pericardium and the foreign body. Because many of these patients were young, we empirically elected to interpose intercostal muscles and periosteum between heart and prosthesis as a buffer and in case the prosthesis had to be removed later. Such a partition might then prevent recurrence of mediastinal shift. Pulse rate and blood pressure were carefully monitored during the insertion of the prostheses as well as during the earlier suture fixation of the pericardium to the sternum to identify possible impairment of cardiac function. The ribs were next laced together with multiple, staggered heavy Vicryl (Ethicon) sutures. The volumes of prostheses placed varied from 750 mL to 1,260 mL. Chest tubes were avoided.

Two of this last group of patients (patients 6 and 9) suffered from problems of persistent severe malacia after repositioning had been accomplished. In 1 (patient 9) attempt was made to manage this with the placement of a long T tube. However, the patient suffered respiratory failure postoperatively, required intubation and ventilation, and, after aortic division and bypass grafting, died of bronchopneumonia. In the other patient (patient 6), after repositioning, malacia was so extensive that carinal resection was performed. Further, some of the anterior vertebral body against which the compressed bronchi were draped was removed to provide a groove for the airway. The patient nonetheless showed continued airway obstruction and compression, and after placement of an aortic bypass graft, aortic division was performed with further tracheobronchial resection. Pericardiotomy was also required after one of the procedures to relieve tamponade due to pericardial fluid and blood. This patient died postoperatively of respiratory failure with massive, viscid casts recurring in the bronchial tree.

Results of Treatment

Clinical Observations

As noted, our initial patient died after the attempt to decompress her airway by aortic division and, additionally, by left main bronchial resection, without mediastinal repositioning. The patient, with one lobe remaining, had pulmonary insufficiency.

The 10 remaining patients all underwent repositioning of the mediastinum, with placement of filling prostheses

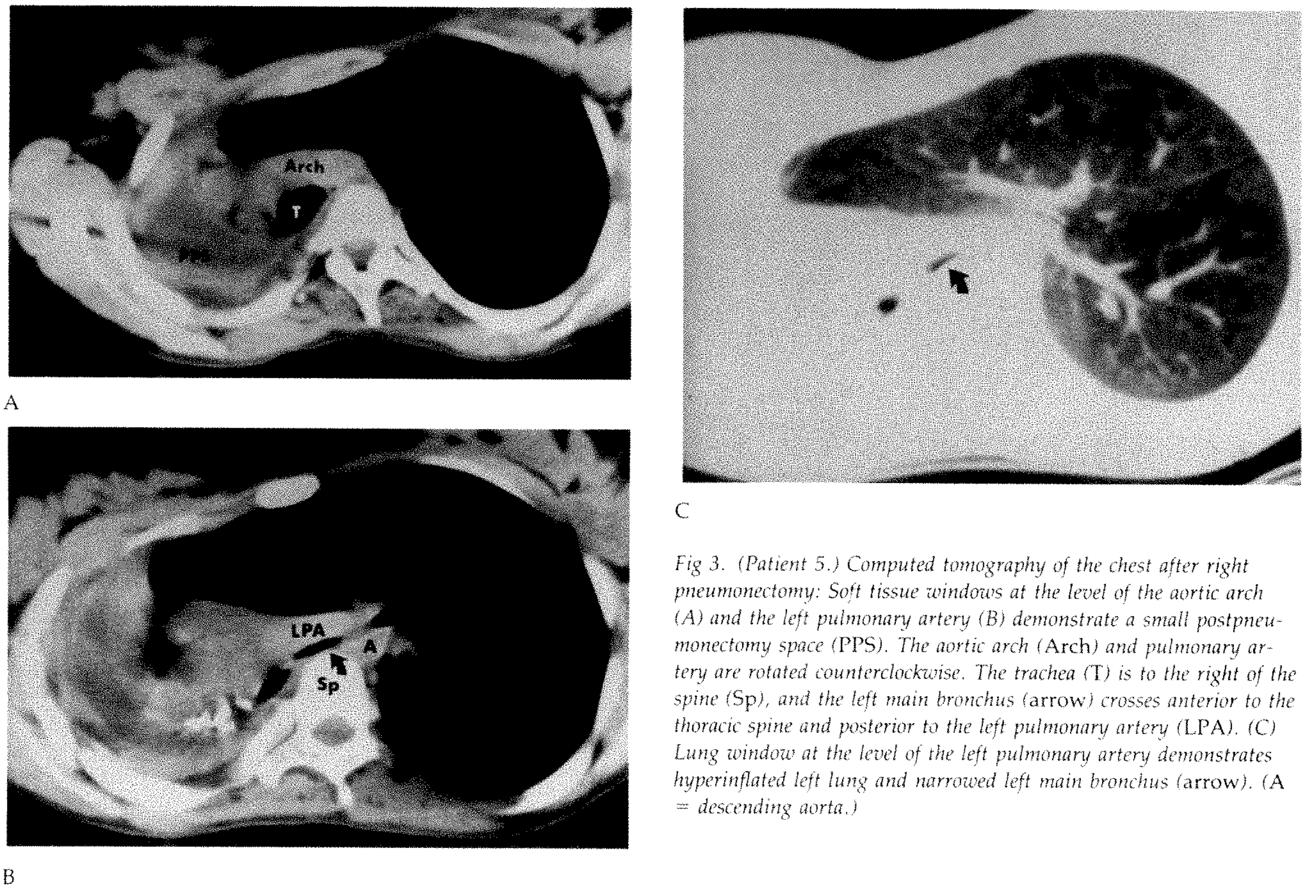


Fig 3. *(Patient 5.) Computed tomography of the chest after right pneumonectomy: Soft tissue windows at the level of the aortic arch (A) and the left pulmonary artery (B) demonstrate a small postpneumonectomy space* (PPS). *The aortic arch* (Arch) *and pulmonary artery are rotated counterclockwise. The trachea* (T) *is to the right of the spine* (Sp), *and the left main bronchus* (arrow) *crosses anterior to the thoracic spine and posterior to the left pulmonary artery* (LPA). *(C) Lung window at the level of the left pulmonary artery demonstrates hyperinflated left lung and narrowed left main bronchus* (arrow). *(A = descending aorta.)*

in 8 ultimately. In 6 this resulted in an adequate airway immediately after operation. In 1 additional patient (patient 7) there was some residual collapse of bronchi, but the airway appeared to be acceptable. The remaining 3 patients had severe degrees of malacia evident in the tracheobronchial tree after mediastinal replacement and, therefore, had additional procedures done. In 2, tracheobronchial resection was accomplished and, in both, aortic division with bypass was performed. One of these patients (patient 2) has survived and is doing well nearly 6 years after operation. The other (patient 6) died postoperatively. The third patient of this group (patient 9) required airway stenting postoperatively, then aortic division, but died postoperatively.

Five of the 6 patients (patients 3, 4, 5, 10, and 11) who underwent mediastinal repositioning with placement of prostheses (1 of whom had the prosthesis placed at a second operation) are currently doing well and are fully active with good airways. The length of follow-up ranges from 5 months to 6 years. The sixth patient (patient 8) in this group had narrow respiratory margins and did well initially, but bronchospasm developed in him just over 1 month after hospital discharge. He was reported to have responded well to bronchodilator therapy and was found to have a patent and stable airway bronchoscopically. Just before discharge from the hospital where he was receiving treatment, he died suddenly. The clinical diagnosis was pulmonary embolism, but no autopsy was obtained (Table 4).

Postoperative Images

In the 8 patients who had repositioning with prostheses (patients 3–5 and 7–11), an immediate postoperative chest film revealed a midline or nearly midline trachea (Fig 8). Six of the 8 patients who had repositioning with prostheses had postoperative CT (patients 4, 5, 7, 8, 10, and 11). Air and fluid were noted surrounding the prostheses in the operated hemithorax. A muscle flap could be discerned against the mediastinum in each patient. Reorientation of the heart and great vessels to a midline position was observed. Individual bronchi were observed to be patent and free of compression (Fig 9). In 2 patients (patients 7 and 10) slight residual narrowing was noted.

Pulmonary Function Studies

Seven patients had expiratory flow volume loops done before and after surgical correction (see Table 2). The two consistent changes, occurring in every patient, were an increase in the peak expiratory flow rate (Fig 10A) and an improvement in the FEV_1/FVC percent ratio ($p < 0.05$) (Fig 10B). The vital capacity decreased in 5 patients; the FEV_1 improved in 4 patients, decreasing in 3 patients. In each patient in whom the FEV_1 decreased there was a large fall in the FVC as well as a resultant improvement in the

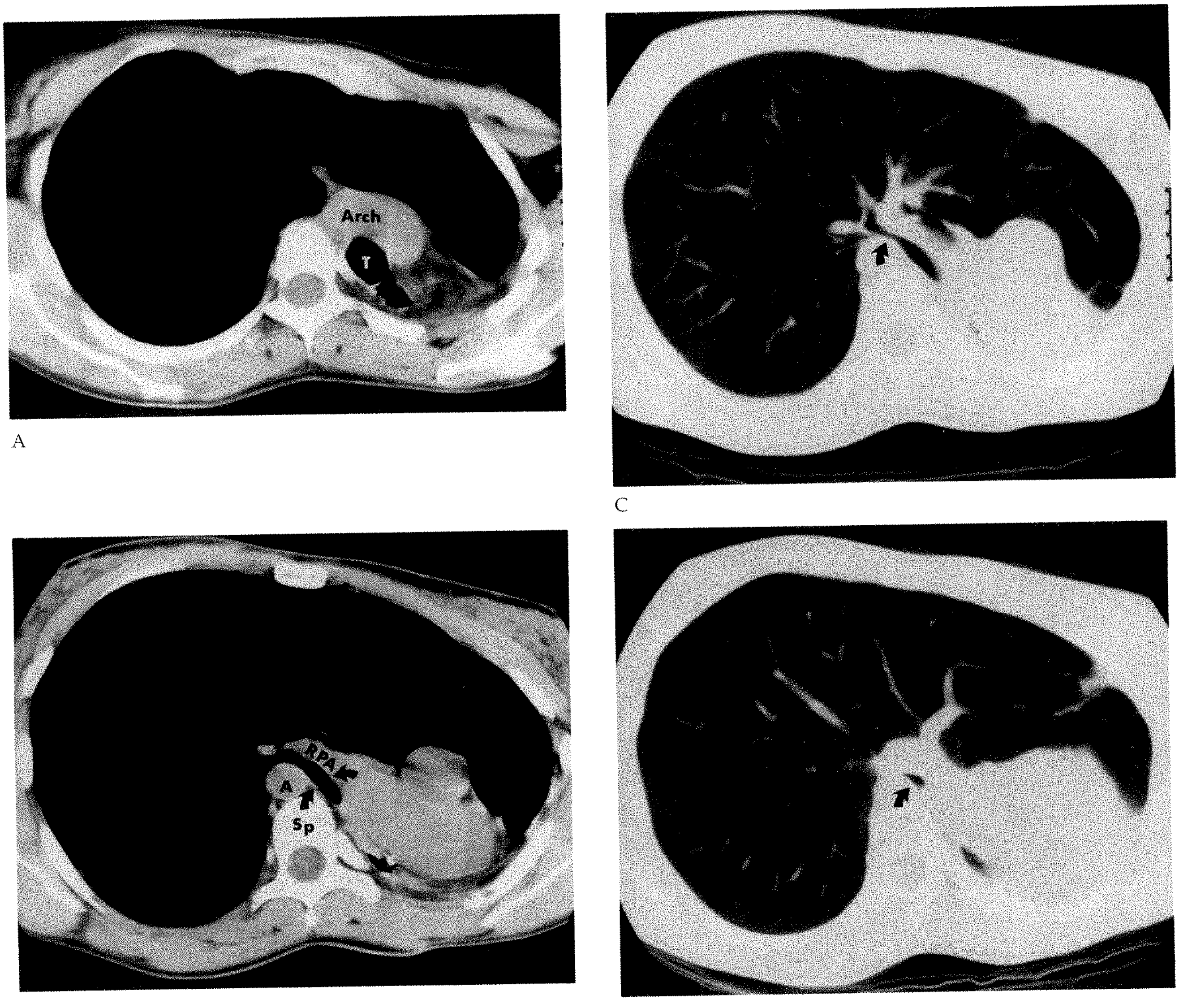


Fig 4. (Patient 11.) Computed tomography of the chest after left pneumonectomy: soft tissue windows at the level of the aortic arch (A) and the right pulmonary artery (B) demonstrate clockwise rotation of the great vessels. There is no identifiable postpneumonectomy space. The trachea (T) is to the left of the spine (Sp), and the right main bronchus crosses into the right hemithorax anterior to the descending aorta (A) and spine and posterior to the right pulmonary artery (RPA). Lung windows at the level of the right upper lobe bronchus (C) and bronchus intermedius (D) demonstrate narrowing of the bronchi (arrows) between the right pulmonary artery and the aorta and spine. (Arch = aortic arch.)

FEV_1/FVC percent ratio. The mean rose from 0.52 to 0.75. In 5 patients a plateau of flow that is characteristic of upper airway obstruction was noted preoperatively and was no longer present in the postoperative studies (Fig 11). Total lung capacity measured in 4 patients preoperatively and postoperatively (see Table 3) decreased very markedly by an average of 46% (range, 21% to 78%) ($p <$ 0.05) of the preoperative value. Residual volume decreased by 60% of the preoperative value. The residual volume/total lung capacity ratio fell markedly in the 4 patients in whom it was measured, from 0.54 to 0.40 (Fig 10C).

Bronchoscopy

Bronchoscopy was repeated through the endotracheal tube intraoperatively after repositioning, again before discharge, and in later follow-up when feasible. It is usually possible to assess the success of the procedure in reopening the airway immediately. If serious malacia is present, this can usually be identified at once and it is little likely to improve further even if there is some initial gross betterment of the airway.

Comment

The rarity of occurrence of postpneumonectomy syndrome is fortunate, because it continues to present major problems in diagnosis and therapy. It is of note that only 2 of our 11 patients underwent pneumonectomy in childhood, which has been thought to be a characteristic component of the syndrome. Examination of serial radiographs after pneumonectomy demonstrated that the mediastinal shift occurred within months of the pneumonectomy in some. Symptoms followed soon thereafter in a progressive and severely disabling course. In other patients the evolution of symptoms has been slower (see Table 1).

Airway obstruction clearly results from mediastinal displacement. After right pneumonectomy, the mediastinum moves to the right and posteriorly as viewed on CT. Because of the attachments of the heart to the great vessels, there is counterclockwise rotation of the heart and great vessels posteriorly as viewed on CT. The left lung herniates into the right anterior portion of the chest. The realignment of intrathoracic structures results in tracheal displacement to the right and compression of the left main bronchus and sometimes the distal trachea as it angles beneath the aorta and is flattened against the vertebral column or against the descending aorta as well. The pulmonary artery is elongated and lies tightly against the anterior wall of the compressed bronchus (see Fig 5). Tracheobronchial compression has also been noted in the analogous situation of displacement and rotation of the heart due to right lung agenesis [10–13].

Similar anatomic distortion after left pneumonectomy occurs in the presence of a right aortic arch. In this case, clockwise rotation of the mediastinum is seen with the trachea pulled to the left and the right main bronchus compressed, overlying the vertebral column or aorta. Because the right main bronchus is so much shorter than the left, it is not uncommon to find that the right upper lobe bronchus and the bronchus intermedius are also compressed against the vertebral column.

Radiographic demonstration of the intrathoracic realignment of the lung and mediastinum is an integral part of the diagnostic evaluation of postpneumonectomy syndrome. Multimodality imaging is recommended to establish the diagnosis and delineate its elements. Conventional chest radiography can establish the marked lateral and posterior displacement of the trachea and mediastinum toward the side of the pneumonectomy and concurrent herniation and hyperinflation of the contralateral lung. The onset of symptoms often coincides with the development of excessive mediastinal shift.

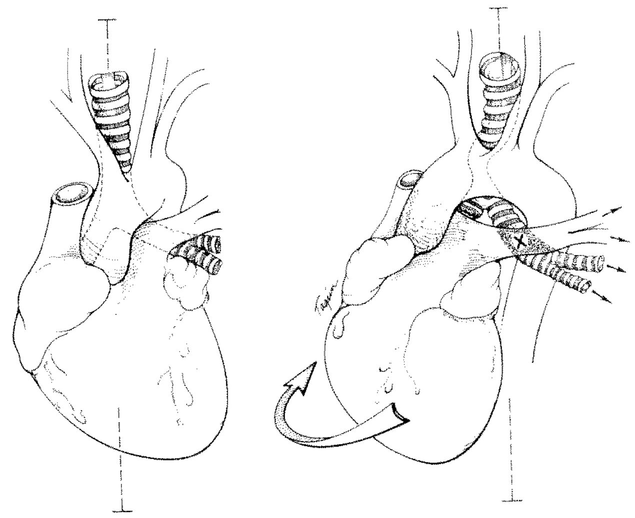


Fig 5. Diagram showing right lateral displacement and posterior rotation of heart and aortic arch after right pneumonectomy with left-sided arch. The dashed vertical line *indicates the midline. The trachea and carina are displaced to the right and posteriorly by the rotated aortic arch, with left main bronchial compression between the left pulmonary artery and descending aorta or against the vertebral spine. A "mirror-image" situation may follow left pneumonectomy in the presence of right aortic arch.*

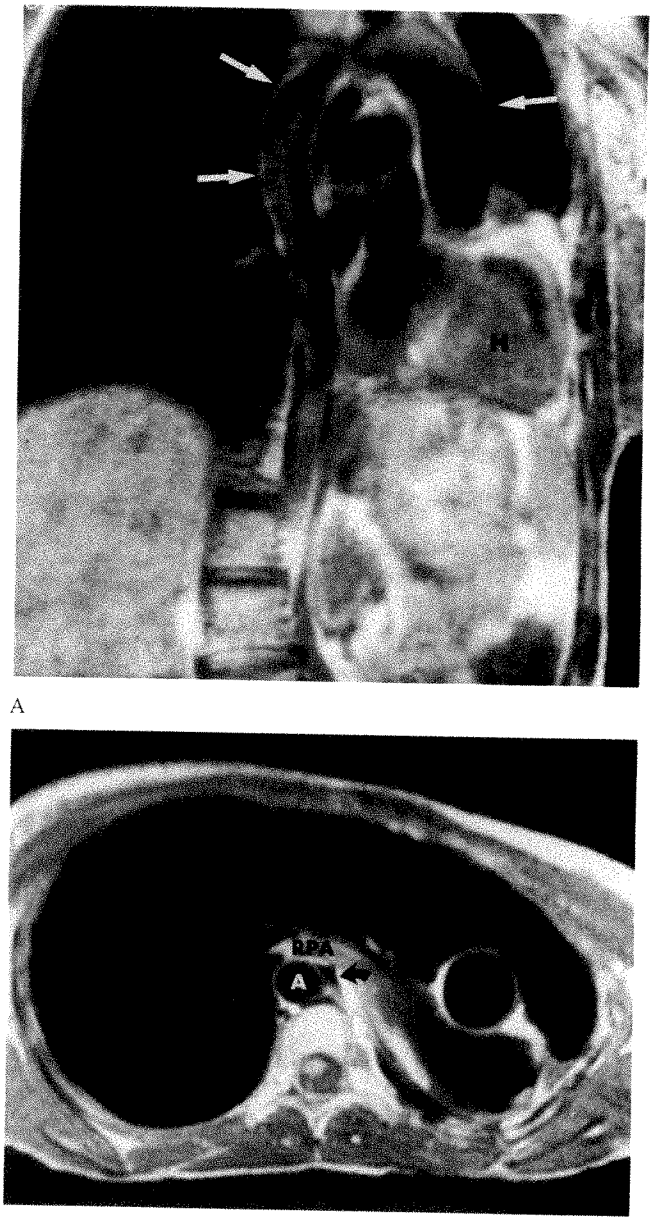


Fig 6. (Patient 11.) Magnetic resonance imaging of the chest after left pneumonectomy: (A) T1-weighted coronal scan of the chest demonstrates a right-sided aortic arch (arrows) *and shift of the heart* (H) *against the left chest wall. (B) T1-weighted axial image demonstrates the right main bronchus* (arrow) *narrowed between the right pulmonary artery* (RPA) *anteriorly and the aorta* (A) *posteriorly.*

Computed tomography of the chest is essential to

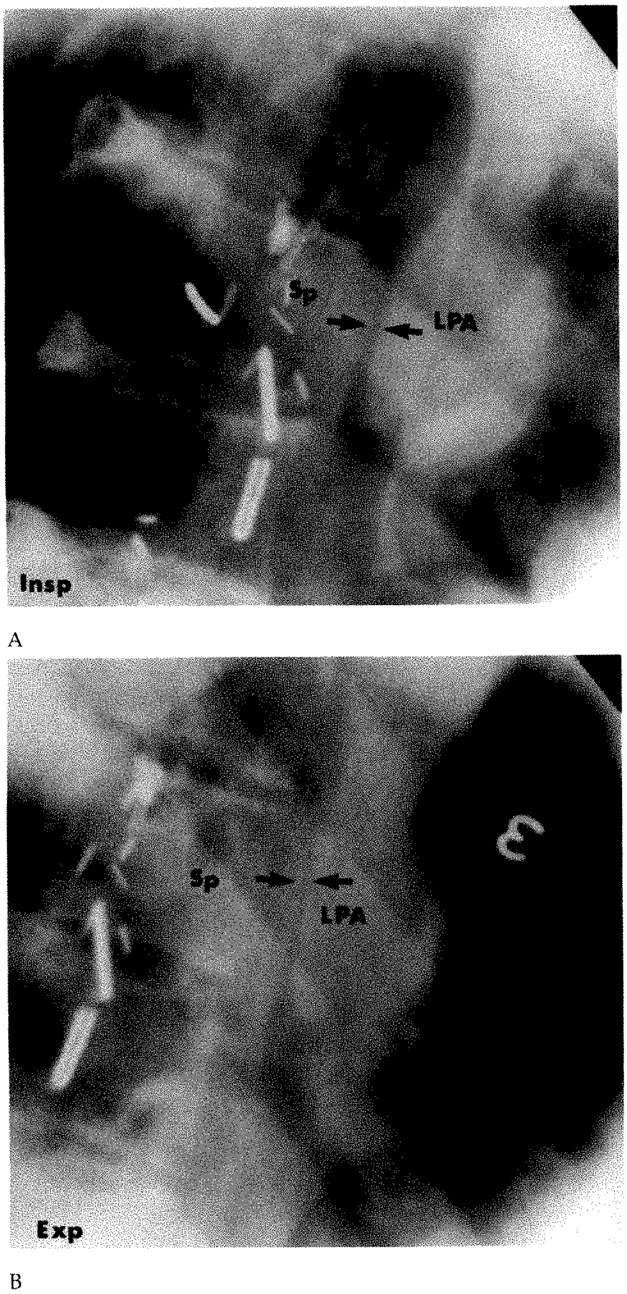


Fig 7. (Patient 5.) Fluoroscopy of the chest after right pneumonectomy: Lateral projection in inspiration (A) and expiration (B) demonstrates narrowing of the left main bronchus between the left pulmonary artery (LPA) *anteriorly and the spine* (Sp) *posteriorly. Complete obstruction of the left main bronchus is noted on the expiratory view (B).* (Exp = *expiration;* Insp = *inspiration.)*

Table 4. Postpneumonectomy Syndrome: Results of Surgical Treatment

	Airway		
Result	Compressed Only	Malacic Also	All Cases
Dead			4
Postop	0	3	
Late	1	0	
Alive			7
Well	5	1	
Dyspneic	1	0	
Total	7	4	11

demonstrate the counterclockwise rotation of the heart and great vessels in reference to the spine after right pneumonectomy and the clockwise rotation that occurs after left pneumonectomy. The presence of a right-sided aortic arch in the setting of left pneumonectomy, suspected on plain films, is confirmed by CT. The exact site of bronchial obstruction can also be detected by CT. The relationship of the pulmonary artery and aorta and spine to the narrowed bronchus or bronchi is readily determined. Inspiratory and expiratory images of the affected bronchi may demonstrate collapse in bronchi not well seen by fluoroscopy. Although conventional linear tomography provides a longitudinal view of the narrowed trachea and bronchus, precise information regarding the mediastinal vascular realignment is lacking and is best demonstrated by CT.

Magnetic resonance imaging is useful in several regards. Multiplanar imaging provides images in the coronal, sagittal, and axial planes. Mediastinal vessels, trachea, and large central bronchi are readily visible. Cine magnetic resonance images provide information regarding the effect of pulsatile vessels on adjacent bronchi. Angiography of the great vessels is usually not indicated

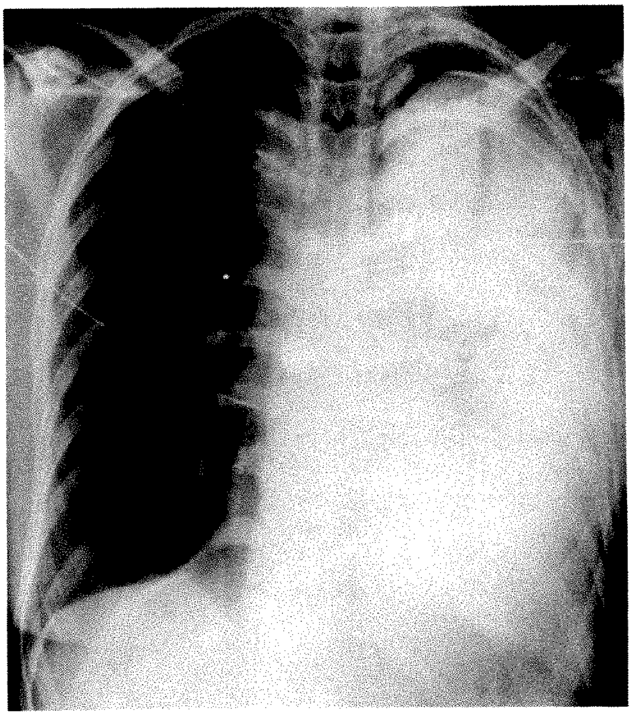


Fig 8. (Patient 11.) Postoperative anteroposterior chest film after repositioning of the mediastinum with breast implants following prior left pneumonectomy. The trachea is midline in position. Air is noted outlining the implants in the left hemithorax.

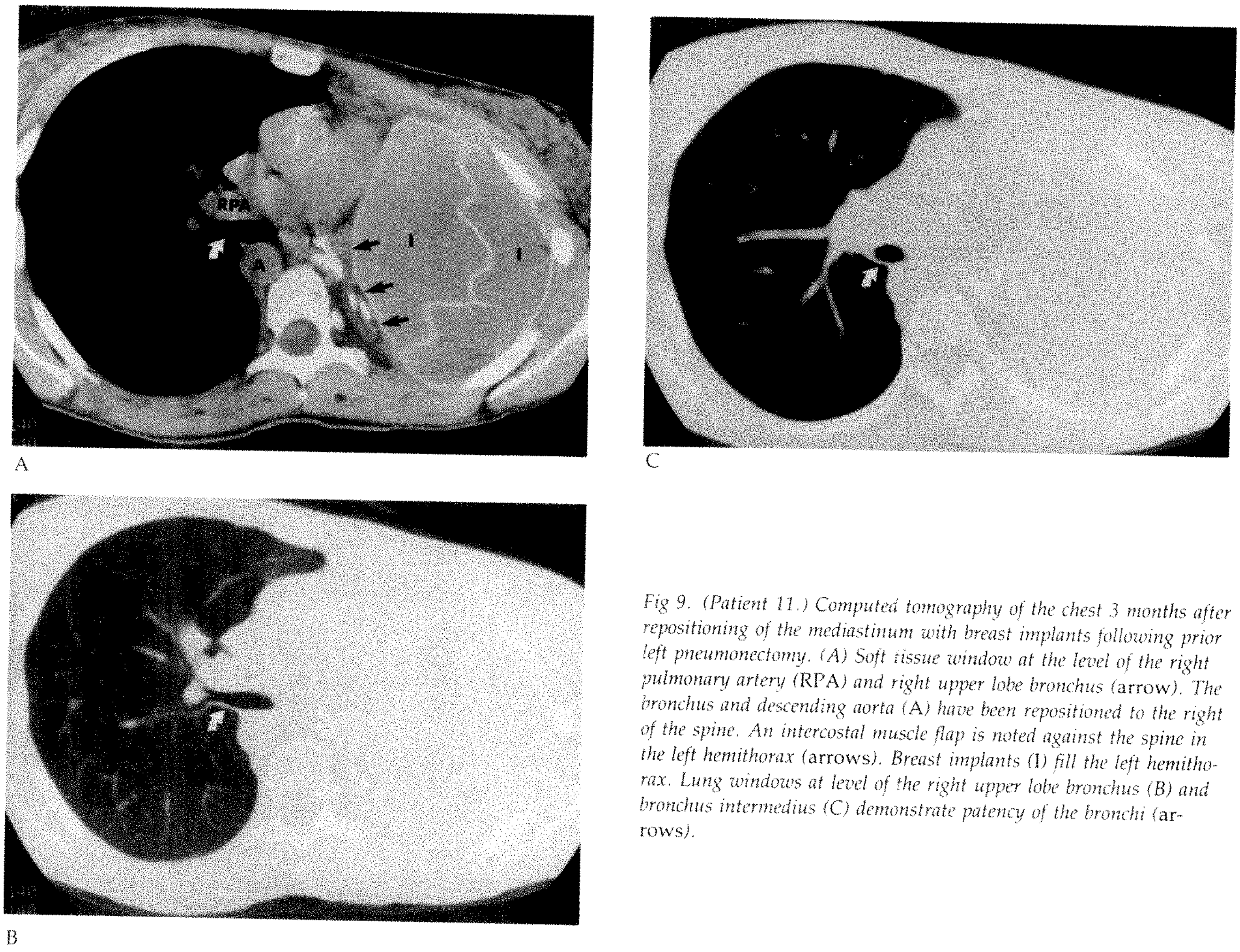


Fig 9. (Patient 11.) Computed tomography of the chest 3 months after repositioning of the mediastinum with breast implants following prior left pneumonectomy. (A) Soft tissue window at the level of the right pulmonary artery (RPA) *and right upper lobe bronchus* (arrow). *The bronchus and descending aorta* (A) *have been repositioned to the right of the spine. An intercostal muscle flap is noted against the spine in the left hemithorax* (arrows). *Breast implants* (I) *fill the left hemithorax. Lung windows at level of the right upper lobe bronchus (B) and bronchus intermedius (C) demonstrate patency of the bronchi* (arrows).

in the initial workup, but may become useful if aortic bypass is contemplated.

The radiographic determination of tracheobronchomalacia is more difficult than establishing the mediastinal anatomic alignment. Interestingly, bronchomalacia was only observed in those patients in whom the bronchus was interposed between the pulmonary artery and the aorta. However, malacia was not present in every instance of this relationship. Bronchomalacia was not present when the bronchus was interposed between the pulmonary artery and the spine (patients 5 and 8). Fluoroscopy is recommended to evaluate for malacia preoperatively, and correctly identified all of the patients with malacia. Although fluoroscopy was very sensitive, it was not very specific. In 4 patients in whom malacia was thought to be present, once the fixed obstruction was removed, the bronchi remained patent.

Immediately after mediastinal repositioning, daily chest radiographs are recommended to assess mediastinal position and the status of the remaining lung. Baseline CT and posteroanterior and lateral chest radiographs are recommended before discharge from the hospital. In cases complicated by postoperative pneumonia, tracheobronchomalacia, or mediastinal slippage, chest CT may be useful to reestablish the anatomic relationships.

The reported experience of attempts at surgical correction of the syndrome consists of single cases treated by a variety of methods with varying results [1–4, 7, 8, 10, 11]. We believe that surgical correction is best accomplished by replacement of the mediastinum to normal relationships to allow the compromised airway to return to its normal position and patency. Our experience with recurrence in 2 patients indicates that simple replacement and suture fixation of the mediastinum is undependable, despite an instance of its success [14]. The empty hemithorax must be filled to prevent recurrence of the disorder. We used silicone breast prostheses as a convenient filler material, as reported previously [3, 8]. Other materials have been used including plastic balls prophylactically and therapeutically [1–3, 15]. Rasch and associates [4] recently described the use of an expandable prosthesis in a 5-month-old infant, which has the advantages of being adjustable postoperatively and, also, with growth. Suspension of the pulmonary artery or aortic arch has usually produced only transient improvement [1, 2, 12].

The benefit from repositioning the mediastinum is

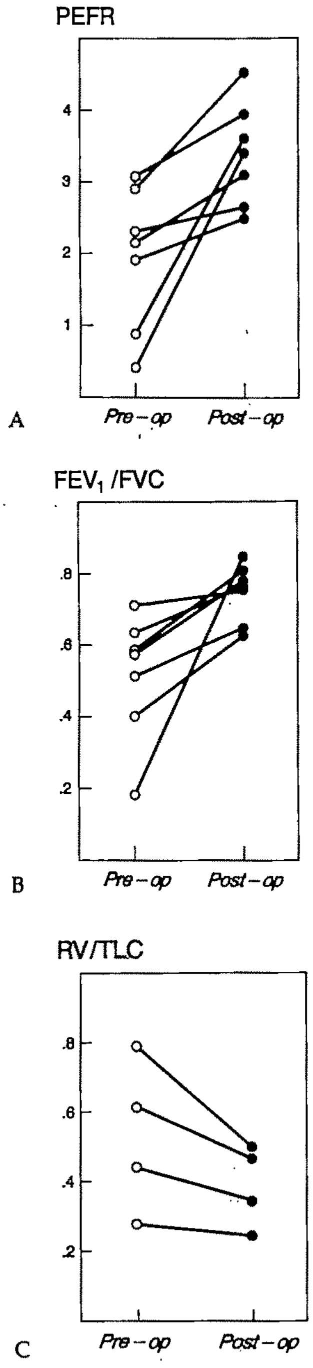


Fig 10. (A) Peak expiratory flow rates (PEFR; liters/second) preoperatively and postoperatively in the last 7 consecutive patients who survived operation. All improved. (B) Forced expiratory volume in 1 second (FEV_1) as percent of forced vital capacity (FVC) in these 7 patients preoperatively and postoperatively. All improved variably. (C) Ratio of residual volume (RV) to total lung capacity (TLC) measured preoperatively and postoperatively in the last 4 patients surviving operation. Residual volume decreased in all as a percent of total lung capacity.

derived not only from relief of mechanical obstruction of the bronchial tree, but from correction of overdistention of the herniated and overexpanded lung. The pulmonary function changes demonstrated these two separate alterations, an improvement in flow rates and a decrease in hyperinflation. The flow rate improvement was reflected in both the increased peak expiratory flow rate and the FEV_1/FVC percent ratio. The former was associated with the loss of the upper airway obstruction plateau and was primarily due to the relief of tracheal compression. The improvement in FEV_1/FVC ratio from a moderately obstructed value of 0.52 to a value in the normal range of 0.75 is due to several factors. First, the decrease in FVC due to relief of hyperinflation was always greater in absolute amount than the decrease in FEV_1. Second, upper airway obstruction was so severe in 3 patients that relief of tracheal compression also resulted in an increased FEV_1. These 3 patients showed the greatest absolute increase in peak expiratory flow rate. Third, it is possible that the severity of the hyperinflation inhibited elastic recoil of the lung. There was a very marked decrease in all static lung volumes, the total lung capacity, functional residual capacity, and residual volume. Total lung capacity showed the greatest absolute decrease, resulting in a decreased residual volume/total lung capacity ratio. Both total lung capacity and residual volume were within the expected postpneumonectomy range after surgical correction. Wasserman and colleagues [8] quantitated similar improvement in their patient.

Bronchoscopy shows not only patency of the compressed bronchus after successful repositioning in the absence of secondary bronchomalacia, but a degree of unkinking of the bronchial tree. This is most noted after left pneumonectomy with right aortic arch where the earlier branching bronchial tree is itself splayed over the vertebral column or descending aorta.

Our experience also demonstrates that, in addition to airway compression by mediastinal displacement, a substantial group of patients may have development of severe malacic changes in their airways. In 2 the interval between the original operation and the clinical presentation had been 8 and 18 years. In a third the interval was

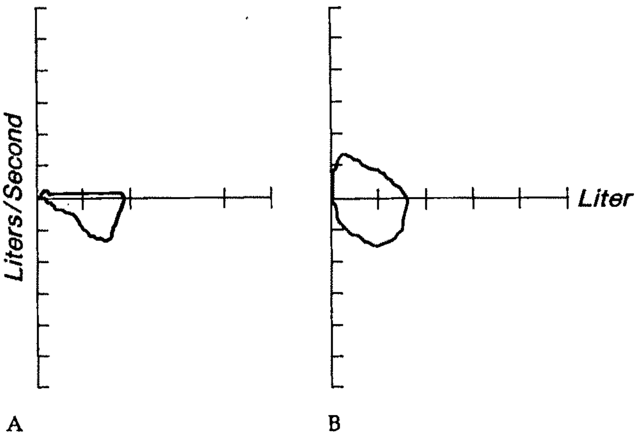


Fig 11. (Patient 5.) (A) Preoperative forced expiratory volume in 1 second, 0.35 L; forced vital capacity, 1.78 L; very marked plateau. (B) Postoperative forced expiratory volume in 1 second, 1.32 L; forced vital capacity, 1.44 L; normal shape of flow volume loop.

only 17 months. This patient, however, had possibly an additional factor from trauma to the airway and prior tracheal repair. A fourth patient in this category with some residual collapse after repositioning had only a 2-year interval after pneumonectomy. It is difficult to know what factors produce this additional disability. In these patients, simple mediastinal replacement and fixation by filler material seems to be insufficient. We do not know at present whether it would be preferable to attempt to manage such patients after repositioning of the mediastinum by placement of bronchial stents, either internal or specially constructed T tubes. A potential for stent erosion may indeed exist. Drastic procedures such as aortic division with or without vertebral tailoring and airway resection, individualized for each patient, have had variable success (patients 2 and 6) [7, 10].

It is also not at all certain whether it is necessary to suture the pericardium to the undersurface of the sternum once it has been elected to place prostheses within the empty hemithorax. Our addition of a mediastinal partition with intercostal muscle and periosteum between prostheses and pericardium may also be unnecessary. Their use was based on experiences with older prosthetic filler materials in collapse procedures of another era, as well as on general observations of unpredictable long-term problems with potentially erosive foreign materials. In view of recent concerns about prostheses containing silicone gel, saline-filled containers will be used in future patients.

Unfortunately, at present there are no clear-cut predictors of the occurrence of postpneumonectomy syndrome. The incidence would seem to be rare enough so that prophylactic steps that might add complexity to pneumonectomy do not appear to be justified [15]. There is indication, however, from this limited series, that correction of the syndrome, once it is identified and has become symptomatic, should be accomplished promptly to minimize the chance for potentially lethal malacia to complicate the syndrome further. When airway stability and patency are achieved and maintained by mediastinal repositioning (and prostheses), and malacia is not serious, the outlook appears to be quite favorable.

References

1. Adams HD, Junod FL, Aberdeen E, Johnson J. Severe airway obstruction caused by mediastinal displacement after right pneumonectomy in a child. J Thorac Cardiovasc Surg 1972; 63:534–9.
2. Park CD, Waldausen JA, Friedman S, Aberdeen E, Johnson J. Tracheal compression by the great arteries in the mediastinum. Arch Surg 1971;103:626–32.
3. Powell RW, Luck SR, Raffensperger VG. Pneumonectomy in infants and children: the use of a prosthesis to prevent mediastinal shift and its complications. J Pediatr Surg 1979; 14:231–7.
4. Rasch DK, Grover FL, Schnapf BM, Clarke E, Pollard TG. Right pneumonectomy syndrome in infancy treated with an expandable prosthesis. Ann Thorac Surg 1990;50:127–9.
5. Shepard JO, Grillo HC, McLoud TC, Dedrick CG, Spizarny DL. Right pneumonectomy syndrome: radiologic findings and CT correlation. Radiology 1986;161:661–4.
6. Stolar C, Verdon W, Reyes C. Right pneumonectomy syndrome: a lethal complication of lung resection in a newborn with cystic adenomatoid malformation. J Pediatr Surg 1988; 23:1180–3.
7. Szarnicki R, Maurseth K, de Leval M, Stark J. Tracheal compression by the aortic arch following right pneumonectomy in infancy. Ann Thorac Surg 1978;25:231–5.
8. Wasserman K, Jamplis RW, Lash H, Brown HV, Cleary MG, Lafair J. Post pneumonectomy syndrome: surgical correction using Silastic implants. Chest 1979;75:78–80.
9. Quillin SP, Shackelford GD. Post pneumonectomy syndrome after left lung resection. Radiology 1991;179:100–2.
10. Harrison MR, Hendren WH. Agenesis of the lung complicated by vascular compression and bronchomalacia. J Pediatr Surg 1975;10:813–7.
11. Maier HC, Gould WJ. Agenesis of the lung with vascular compression of the tracheobronchial tree. J Pediatr 1953;43: 38–42.
12. McCormick TL, Kuhns LR. Tracheal compression by a normal aorta associated with right lung agenesis. Radiology 1979;130:659–60.
13. Wheeler PC, Wolff LJ, Stevens EM. Pseudovascular ring resulting from right lung agenesis, normal aortic arch and patent ductus arteriosus. Am J Roentgenol Radium Ther Nucl Med 1966;98:365–8.
14. Rainer WG. Editorial comment on [8]. Chest 1979;75:80.
15. Johnson J, Kirby CK, Lazatin CS, Cucke JA. The clinical use of a prosthesis to prevent overdistention of the remaining lung following pneumonectomy. J Thorac Surg 1949;18: 164–72.

DISCUSSION

DR VICTOR F. TRASTEK (Rochester, MN): It is indeed a privilege and an honor for me to have the opportunity to discuss Dr Grillo's report on postpneumonectomy syndrome. It is important that Dr Grillo and his group have assembled their considerable experience with this syndrome so that we all can learn how to best treat these patients. Fortunately this is a rare event, though I suspect in varying degrees of severity it may occur more often than we know. Why it occurs is unclear, but the patients are clearly in trouble with compromised airways.

Although our experience is small compared with Dr Grillo's, we agree that making an accurate diagnosis is most important and is best accomplished with the use of computed tomography, pulmonary function tests, and bronchoscopy. More recently we have found the use of fast computed tomographic scanning to be very helpful in evaluating the tracheobronchial tree for obstruction and malacia. Once the diagnosis is confirmed, we also agree that repositioning of the mediastinum should be accomplished and that long-term success depends on the use of a prosthesis to keep the mediastinum from migrating. To this end we currently recommend, as Dr Grillo did, expandable saline prostheses. Finally, in the patient with a malacic segment, success is very difficult to attain. Treatment of these patients must be individualized. Hopefully internal stenting and in very selected cases resection will be helpful.

In closing I commend Dr Grillo and his group for their role in the evolution of treating postpneumonectomy syndrome. I have three questions.

First, this is obviously a rare event as we do not see it very often compared with the number of pneumonectomies that are performed. Do you have any thoughts or insight into why it occurs? Second, do you still advocate, and I think you do judging by your discussion, placing the prostheses extrapleurally? This seems to add a fair amount of dissection to the procedure. And third, you had no infections in the group of patients with prostheses. Obviously this is a concern if it occurs. Do you do anything special to prevent infection?

DR GRILLO: Thank you very much, Dr Trastek, for your kind comments. We do not have an insight into why this occurs. Our first patients had pneumonectomy in childhood or as young adults. I thought that young adults were behaving, perhaps because of the lability of their collagen, like infants or children. That is certainly not the case. Later patients were in their 40s and 50s. I do not know the answer.

There were proposals long ago in the literature to put in prophylactic filler to prevent shift. Because the syndrome happens so rarely, I would not advise prophylactic filler unless something very simple evolves.

Do we do subcostal plombage? Yes, we do. We thought this might be overkill. However, surgical history tells us that materials such as iodized oil, paraffin, lucite balls, and balls in plastic bags almost all had to be removed after a period of some years for one reason or another. We thought that intercostal myoplasty might provide some extra insurance. These are young people, and it turns out, if you read the newspapers, that this seems not so unwise after all.

We do use prophylactic antibiotics against infection, for whatever that is worth. We avoid chest tubes postoperatively to eliminate avenues of ingress. We do, of course, irrigate the hemithorax thoroughly before closing. Infection has not been a problem thus far.

Dr Trastek mentioned fast computed tomography. We have found inspiratory/expiratory computed tomographic scan extraordinarily useful. It really demonstrates the dynamics graphically, in addition to video fluoroscopy and bronchoscopy. Magnetic resonance imaging also shows the anatomy nicely but it is not as crisp as computed tomography.

DR RALPH O. BUTZ, JR (Hines, IL): I wondered, if you are going to do a subcostal plombage, is it necessary to open the pneumonectomy space too?

DR GRILLO: If you do not open the pneumonectomy space you cannot free up and return the mediastinum to a normal position.

DR THOMAS R. J. TODD (Ottawa, Ont, Canada): Dr Grillo, you and Dr Trastek have touched a bit on the question that I had in mind. I am presuming that in the patients who had malacia that complicated the problem, that malacia was identified postoperatively. I might be wrong on that and I would like to know if you had identified it preoperatively. Do you have any tricks for us other than fast-track scanning, which most of us do not have access to, for identifying the malacia in a reliable way preoperatively?

DR GRILLO: To try to identify malacia we have done inspiratory/expiratory computed tomography. Your radiologist will do these for you if he or she knows what you want. Old-fashioned fluoroscopy of the airways is of some help but must be done by a radiologist who is interested in the problem. Bronchoscopy is performed with a flexible instrument on an awake patient. The patient can be asked to breathe deeply and cough. Cartilages may be so badly compressed that it is difficult to tell by direct observation alone how much substance remains. Therefore, multiple diagnostic maneuvers are useful. After you have done the repositioning, you should withdraw the endotracheal tube a certain distance and perform bronchoscopy again to see what has been accomplished.

DR ROBERT J. GINSBERG (New York, NY): I think you have unwittingly identified a risk group of individuals in whom this syndrome develops. I would think that 90% of pneumonectomies performed in this country are for carcinoma and are done in people over the age of 50 years, whereas 90% of your patients were under the age of 50 years and were operated on for benign disease. Maybe these patients are a high-risk group for this development. There is a method of prophylaxis we are not familiar with. The Japanese have been using repeated injections of sulfur hexafluoride to maintain the mediastinum in the midline after pneumonectomy with some interesting results in long-term pulmonary function. Perhaps in this group of young people one should consider this type of prophylaxis, because it appears as though there may be a significant incidence in this group of patients.

DR GRILLO: I think that is a very pertinent comment. If a method becomes available such as you are describing that would not carry with it undue risks, I think prophylaxis might well be considered in that group.

Revival of the Radial Artery for Coronary Artery Bypass Grafting

Christophe Acar, MD, Victor A. Jebara, MD, Michele Portoghese, MD,
Bernard Beyssen, MD, Jean Yves Pagny, MD, Philippe Grare, MD,
Juan C. Chachques, MD, Jean-Noël Fabiani, MD, Alain Deloche, MD,
Jean Leon Guermonprez, MD, and Alain F. Carpentier, MD, PhD

Department of Cardiovascular Surgery, Hôpital Broussais, Paris, France

Eighteen years after its first introduction for coronary artery revascularization, the radial artery (RA) was reinvestigated because of unexpected good long-term results in the early series. Since July 1989, 104 patients underwent myocardial revascularization using 122 RA grafts (18 patients received two grafts). The left internal mammary artery (IMA) was concomitantly used as a pedicled graft in 100 cases and the right IMA in 19 cases; a free IMA graft was used in 29 cases and a saphenous vein graft in 24 cases. A mean of 2.8 grafts per patient were performed. Nine patients underwent associated procedures: carotid endarterectomy (3), aortic valve replacement (3), Bigelow procedure (1), and mitral valve repair (2). The target artery receiving the RA was the circumflex (n = 59), diagonal (n = 29), right coronary (n = 27), and left anterior descending (n = 7). One patient died (0.96%) and 2 had perioperative myocardial infarct. Sternal wound infection was noted in 3 cases of double IMA implantation. No ischemia of the hand was observed. All patients received diltiazem started intraoperatively and continued after discharge. In addition aspirin (100 mg/day) was given at discharge. Early angiographic controls (<2 weeks) were obtained in the first 50 consecutive patients and revealed 56 of 56 patent RA grafts, 48 of 48 patent left IMA grafts, 11 of 11 patent right IMA grafts, 14 of 18 patent free IMA grafts, and 8 of 9 patent vein grafts. Six patients had localized narrowing of the RA conduit unrelated to the anastomotic lines (spasm). Late angiographic control was obtained after a mean follow-up of 9.2 months in 27 patients; 29 RA grafts were patent (93.5%) and free of spasm and 2 were occluded. This study showed that the RA may be a reasonable alternative to other types of conduits to complement the left IMA.

(Ann Thorac Surg 1992;54:652–60)

Coronary bypass using the radial artery (RA) was first proposed and performed by Carpentier in 1971 [1]. Two years later, he recommended that this technique should be abandoned because of a 35% incidence of narrowing or occlusion of this conduit at control arteriography [2]. He suggested that graft failure was due to a spasm of the denervated artery [2]. In 1987, he received from a referring cardiologist the recent coronary angiogram of a patient in whom the RA examined immediately after the operation was thought to be occluded. Fifteen years later, this artery was actually fully patent with no visible arteriosclerotic lesion (Fig 1). Two other patients belonging to the early series and having shown some degree of obstruction at the control examination after operation were reinvestigated and showed a patent RA conduit (Fig 2).

These observations, together with new antispastic drugs available today, stimulated our group to reinvestigate the technique in carefully selected patients.

Material and Methods

Patient Population

Between July 1989 and December 1991, 104 consecutive patients underwent myocardial revascularization using a radial artery graft. The main reason for using a radial artery was the unsuitability of the saphenous veins in 60 patients (57.7%) due to prior harvesting (n = 18), bilateral stripping (n = 15), or varicose veins (n = 27). There were 84 men and 20 women with a mean age of 60.2 ± 8 years (range, 33 to 77 years). Preoperative patient characteristics were as follows:

Hypertension	66
Diabetes	23
Dyslipemia	47
Multilevel atherosclerosis	
Stenosis of supraaortic trunks	12
Aortoiliac disease	15
Previous vascular operation	15
Angina	
Stable	51
Unstable	53
Prior myocardial infarction	52
Emergency percutaneous transluminal coronary angioplasty failure	5

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Acar, Department of Cardiovascular Surgery, Hôpital Broussais, 96 rue Didot, 75014 Paris, France.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

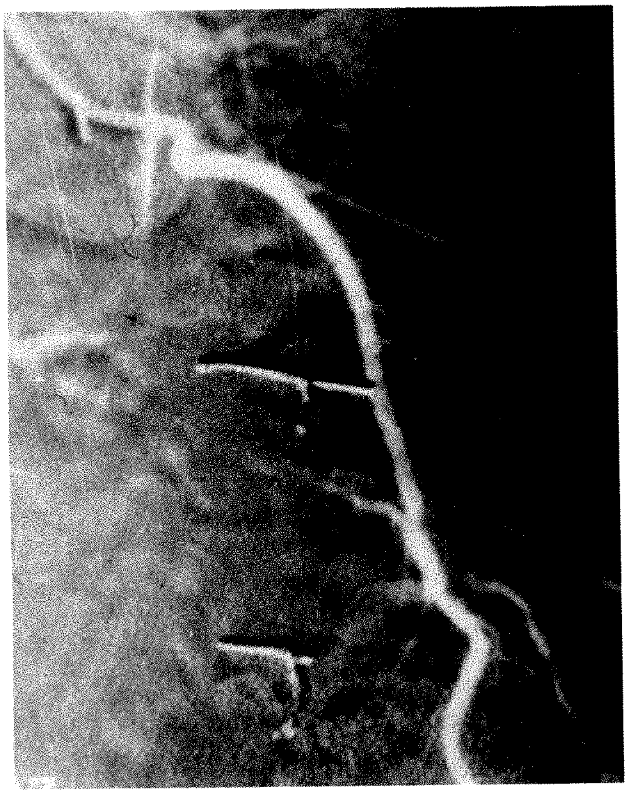


Fig 1. *Radial artery graft to left anterior descending artery at 14 years.*

Reoperation	13
Angiographic ejection fraction	
>0.60	55
0.40–0.60	34
<0.40	40

Fifty-three patients (51.0%) presented with unstable angina and 5 patients (4.8%) were operated on an emergency basis after failure of percutaneous transluminal coronary angioplasty. Thirteen patients (12.5%) presented for redo coronary surgery. Fifteen patients (14.4%) had severely impaired left ventricular function (ejection fraction <0.30).

Harvesting Technique

An Allen test as well as Doppler studies of the forearm were routinely performed before radial artery harvesting. The left forearm was chosen in right-handed individuals (n = 92), the right forearm in the 12 remaining. An incision was made from the wrist to the elbow. The antibrachial fascia was divided and the radial artery dissected from the pulse groove to its proximal segment lying underneath the muscle belly of the brachioradialis reaching the humeral bifurcation. This muscle was retracted without being divided.

The radial artery was removed together with its pedicle including two satellite veins and the surrounding fat tissue. The artery has numerous collateral branches, particularly in its distal portion, which were occluded using surgical clips.

After total mobilization the artery was wrapped with sponges soaked with papaverine and kept circulating. After institution of cardiopulmonary bypass the RA was removed and hydrostatic dilation was undertaken at a gentle pressure using a solution of blood and papaverine (40 mg/L) until a regular aspect of the graft totally free of segmental spasm was obtained. The graft was then stored in the same solution until its use.

Coronary Grafts

A total of 2.8 ± 0.1 coronary bypass grafts per patient were realized. On 104 patients, 122 coronary artery bypass grafts with the RA were performed. Eighteen patients received two bypass grafts using the same radial conduit. Sites of implantation of grafts are listed in Figure 3. The radial artery was anastomosed to the circumflex (n = 59), diagonal (n = 29), right coronary (n = 27), and left anterior descending arteries (n = 7).

The distal anastomosis was performed using a running 7-0 or 8-0 polypropylene suture depending on the thickness of the coronary arterial wall. The proximal anastomosis was realized using side clamping of the aorta. A 4-mm hole was made on the aorta on which the proximal

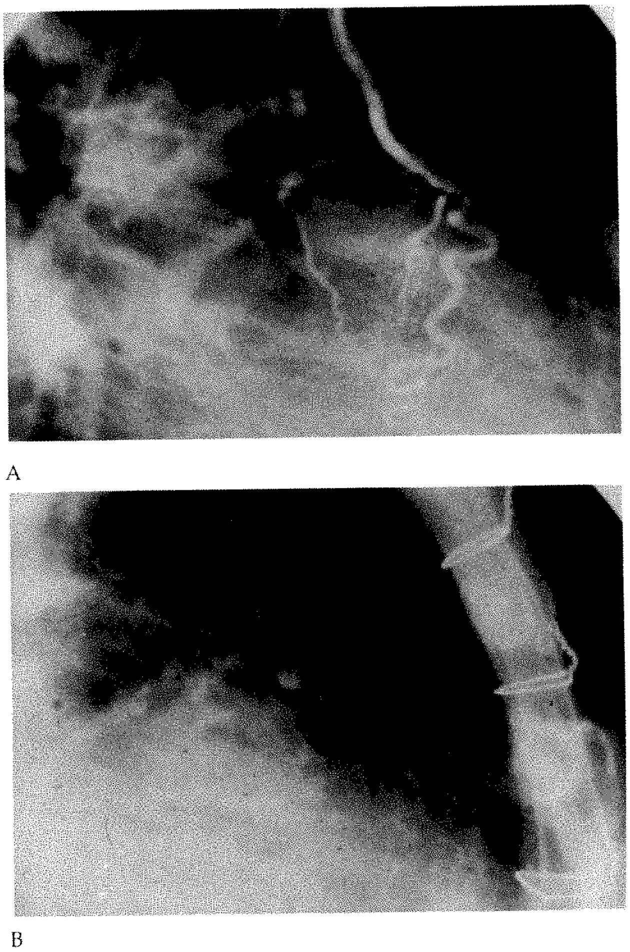


Fig 2. *Radial artery grafts to left anterior descending (A) and diagonal (B) coronary artery at 18 years.*

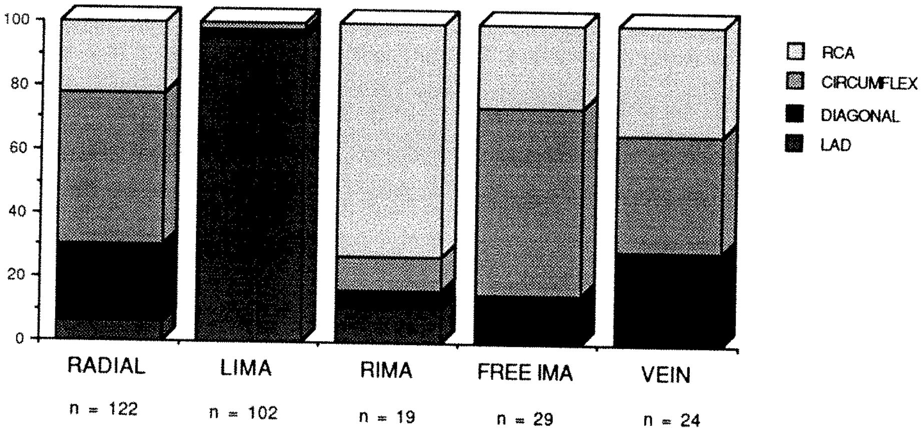


Fig 3. *Implantation sites of grafts.* (IMA = *internal mammary artery;* LAD = *left anterior descending artery;* LIMA = *left IMA;* RCA = *right coronary artery;* RIMA = *right IMA.)*

end of the RA was directly anastomosed using a 7-0 polypropylene suture.

The left internal mammary artery (IMA) was used in 102 cases (pedicled, 100; free, 2) and was anastomosed to the left anterior descending artery in 97 cases. The right IMA was used in 46 cases (pedicled, 19; free, 27). Twenty-four saphenous vein grafts were concomitantly used. Associated procedures were performed in 9 cases: carotid endarterectomy (n = 3), aortic valvular replacement (n = 3), mitral valve repair (n = 2), and Bigelow procedure (n = 1).

Medical Treatment

All patients received intravenous diltiazem started intraoperatively and continued in the intensive care unit at the dose of 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$. This medication was then administered orally throughout the follow-up period (250 mg/day). In addition, low-dose aspirin (100 mg/day), was prescribed starting 1 week after operation.

Control Angiograms

Control angiograms were obtained in the first 50 consecutive patients within 3 weeks after the operation. Selective injections of all grafts were performed using various incidences. Whenever abnormalities of a graft were observed, injections were repeated after in situ instillation of vasodilators (trinitrin) and calcium blockers (nifedipine). All angiographic abnormalities were recorded and results were classified into five subgroups: (1) excellent result, (2) moderate narrowing (<50%), (3) serious localized narrowing (>50%), (4) string sign, defined as a severe and extensive narrowing of the whole body of the graft, and (5) occlusion.

Late control angiograms using the same technique were obtained in all the 27 patients reaching 6 months of follow-up.

Results

Clinical Results

One patient died, for a hospital mortality of 0.96%. Two patients (1.9%) had evidence of perioperative myocardial infarction (1 patient with an occlusion of a free IMA graft and another patient with all patent grafts). Postoperative complications were as follows:

Death	1
Perioperative infarction	2
Need for intraaortic balloon pump	5
Reoperation for bleeding	3
Mediastinitis	3
Hand ischemia	0
Dysesthesia of the thumb	8

Three cases of sternal wound infection were observed in patients with bilateral IMA grafts.

No signs of hand ischemia were observed after RA removal. However, in 8 patients transient dysesthesia of the thumb with no functional abnormalities was noted.

All surviving patients (n = 103) were followed up for a period ranging from 2 to 26 months (mean, 6.9 months). All were alive and free of symptoms. No functional disturbances related to radial artery harvesting were reported.

Control Angiograms

EARLY ANGIOGRAMS. Routine angiographic controls were obtained in the first 50 consecutive patients during the first 3 weeks after the operation. Figure 4 shows the results of these early angiograms.

All 56 RA conduits were patent (100% patency rate at 3 weeks) (Fig 5B). However, a segmental narrowing of the RA conduit was encountered in 6 patients and judged to be moderate in 4 and significant in 2. The location of this narrowing was the proximal segment of the graft in contact with the tip of the angiography catheter in 3 patients (Fig 6) and both the proximal and the distal portion in 3 others (Fig 7A). In situ infusion of vasodilators and calcium blockers resulted in either total regression of the narrowing (n = 1), partial release (n = 2) (see Fig 7), or no modification (n = 3).

All pedicled left and right IMA grafts were patent, for a patency rate of 100% at 3 weeks. However, in 2 patients, an important dicrepency was noted between the size of the right IMA and the target right coronary artery. A serious anastomotic line stenosis was noted in 1 patient.

Among the 18 free IMA grafts, 2 were occluded and two had a string sign; thus the early patency rate of this conduit was 77.8%. Also, four moderate stenoses and one serious stenosis unmodified by in situ instillation of vasodilators were observed in these grafts.

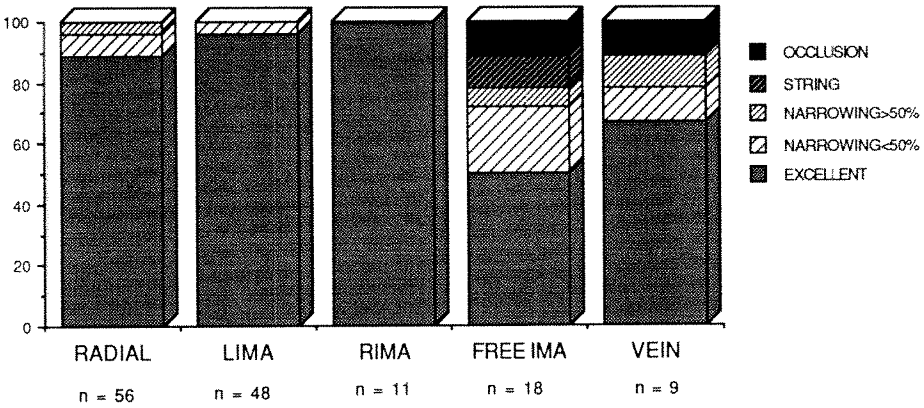


Fig 4. Early angiographic results. (IMA = *internal mammary artery;* LIMA = *left IMA;* RIMA = *right IMA.)*

Eight of nine saphenous vein grafts (88.9%) were patent. One of them had a poor flow with stagnation of the contrast medium (Fig 5B). A stenosis of the vein graft was observed in 2 patients: at the distal anastomosis in 1 patient and at the midportion of the graft in another patient.

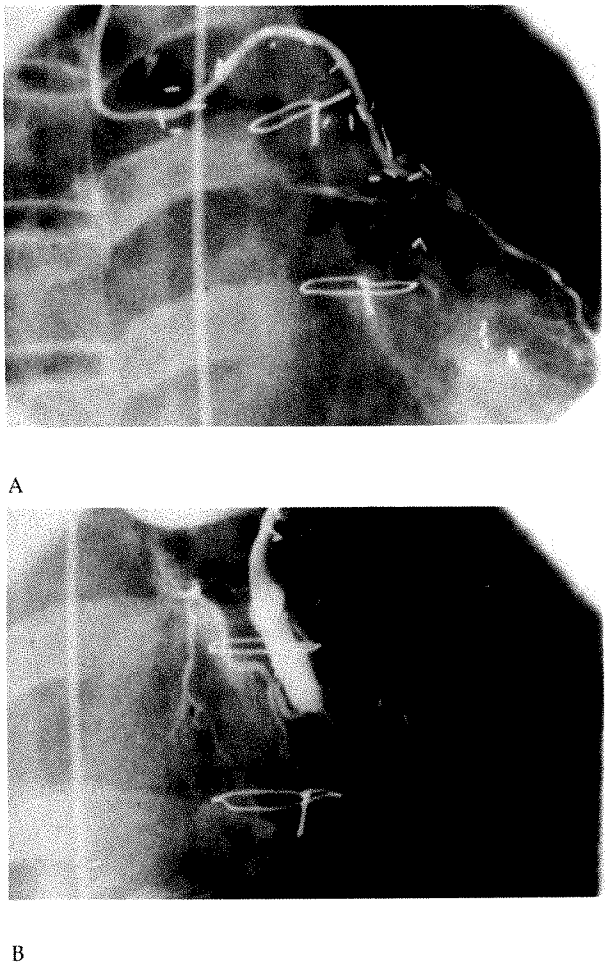


Fig 5. Postoperative angiogram showing the adequate size match between the radial artery and the target diagonal artery (A), contrasting with a dilated hypoperfused vein graft (B).

LATE ANGIOGRAMS. Late angiograms were performed in 27 patients with 31 RA grafts from 6 to 13 months postoperatively (average follow-up, 9.2 months). Figure 8 shows the results of these late angiograms. Among the 31 RA grafts, 29 were patent (93.5%) (Figs 9, 10). All the patent RA grafts were totally free of any abnormality except in 1 case displaying a moderate stenosis of the distal anastomotic line. Among these 29 grafts, 2 had a narrowing on

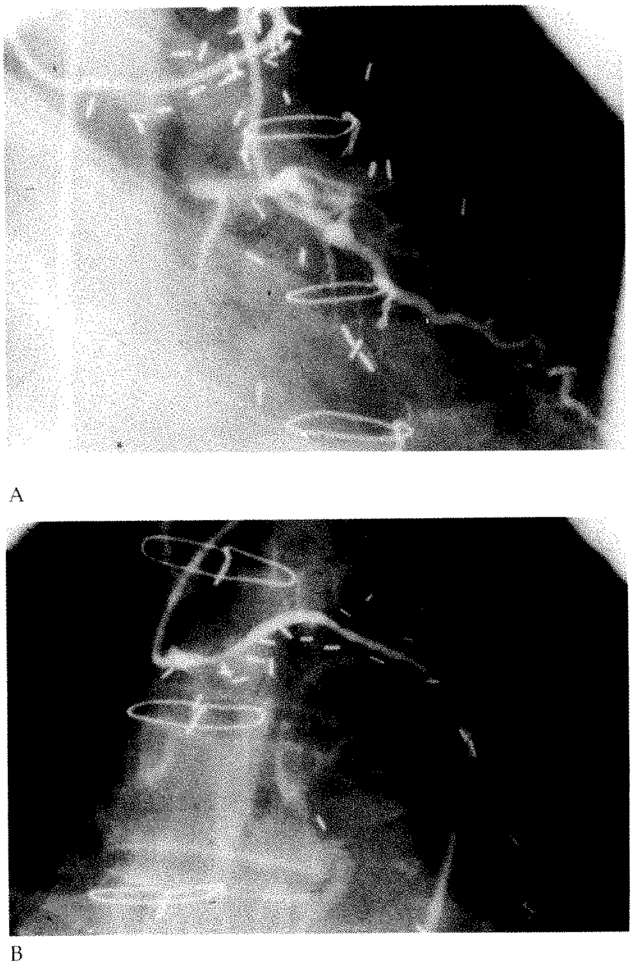


Fig 6. Spasms of radial artery grafts in contact with the tip of the angiography catheter judged to be moderate (A) and serious (B).

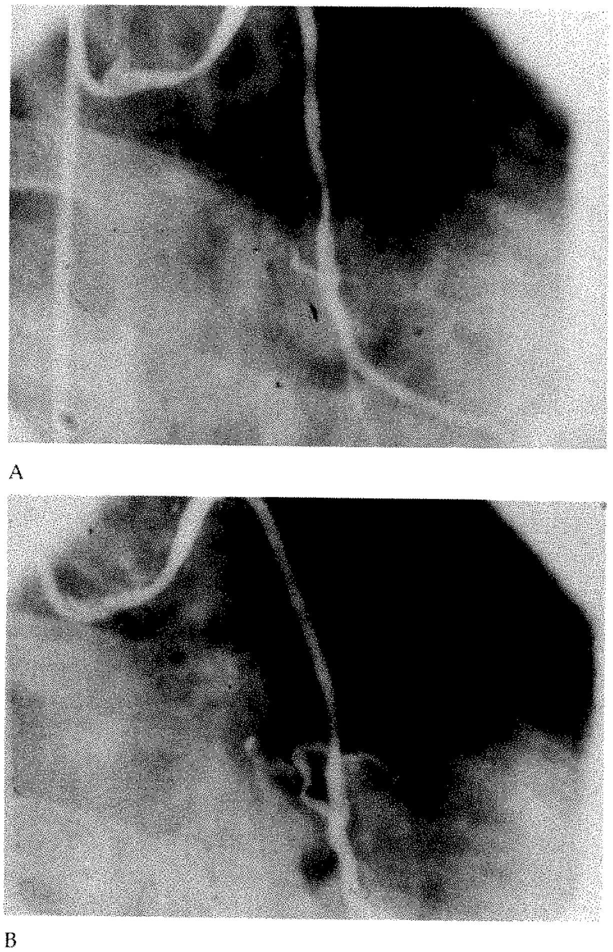


Fig 7. Spasm of both the proximal and the distal portion of a radial artery graft before (A) and after (B) instillation of nitroglycerin resulting in partial release.

the early control angiogram and displayed a perfect result 6 and 12 months later (Fig 11). One of the occluded grafts involved an RA bypass graft constructed on a small diagonal branch with a normal aspect on the early angiogram. This patient had another RA graft performed on the obtuse marginal artery, which was fully patent at 6 months. The other occluded RA in this series involved an RA graft constructed on a severely atherosclerotic left anterior descending artery.

Results of late angiograms of the other types of graft are shown in Figure 8; the patency rate was 100% for the pedicled IMA and 69.3% for the free IMA.

Comment

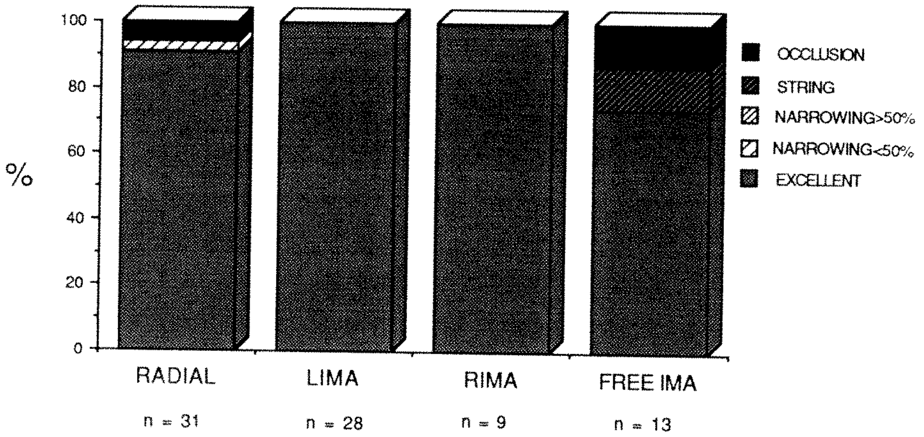
In 1971 Carpentier first advocated the use of the RA for coronary artery bypass [1]. A few years later this technique was abandoned due to an incidence of graft narrowing that was judged to be unacceptable [2]. The exact mechanism of RA occlusion was not clearly elucidated. Microscopic analysis of at least one anatomic specimen after RA graft failure showed an important degree of intimal hyperplasia [3]. On the other hand, Carpentier [2] suggested that "the narrowing of the arterial graft was related to spasm of the denervated artery" and concluded that "the radial artery should not be used in coronary surgery until this physiological problem has been resolved."

Twenty years later, the high incidence of late obstruction of venous bypass grafts together with the increasing interest in total arterial revascularization and the recent advances in antispasm pharmacological agents stimulated us to reinvestigate the use of the RA for coronary bypass grafting. Also, we were encouraged by several patients who had received an RA graft in the early 1970s and in whom control angiograms 15 to 18 years later showed excellent results (see Figs 1, 2).

In this series, 104 patients received 122 RAs as a conduit for coronary bypass grafting. Knowing that most graft occlusions occurred within the first months postoperatively, control angiograms were performed in the early postoperative period (<3 weeks) to obtain a baseline study. Angiograms were repeated 6 to 12 months later to assess the late patency rate of the RA conduits.

Routine early angiograms were obtained in the first 50 consecutive patients. All RA grafts were patent, for a 100% patency rate. All grafts but 6 were totally free of any anatomic abnormality. The narrowing observed on the 6 RA grafts was always distant from the anastomotic lines,

Fig 8. Late angiographic results (9.2 months). (IMA = internal mammary artery; LIMA = left IMA; RIMA = right IMA.)



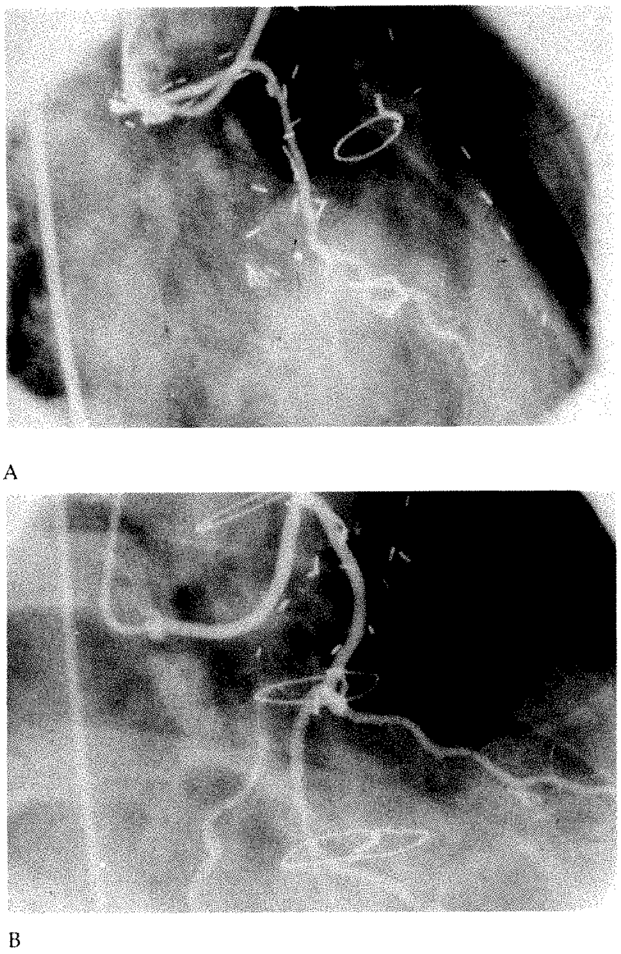


Fig 9. Radial artery grafts to diagonal (A) and obtuse marginal (B) artery at 6 months.

frequently located at the tip of the angiography catheter (see Fig 6) and sensitive to vasodilators in 3 of 6 grafts (see Fig 7). In addition, when examined 6 to 12 months later, 2 grafts that were narrowed at the time of the early control angiogram had recovered a normal aspect (see Fig 11). Therefore, it seems highly probable that these narrowings were due to a segmental spasm of the RA conduits.

The patency rate of the RA conduits at 9 months was 93%, an encouraging figure if one takes into consideration the fact that RA grafts were mostly anastomosed to coronary vessels of secondary importance. The two late obstructions involved either atherosclerotic or small coronary arteries.

As expected early and late control angiograms showed excellent results of the in situ IMA. Left IMA to the left anterior descending and right IMA to the right coronary artery were the two techniques most commonly used in this study (see Fig 3). In contrast, free IMA displayed a poor angiographic result, with only 78% of grafts functional during the postoperative period (see Fig 4). Noteworthy is the fact that free IMA grafts and RA grafts were constructed on the same target coronary vessels (mainly the circumflex system) (see Fig 3). This discrepancy in the results between pedicled IMA and free IMA was also noticed by Dion and associates [4].

In this series, the radial artery for coronary bypass grafting seems to have provided better results than those reported in the early experience. The incidence of graft narrowing or occlusion in our old series including 42 patients was 35% within the 10 months of follow-up [2]. Curtis and associates [3] reported a failure rate of 65% in 29 patients restudied at 7 months. Fisk and co-workers [5] found a 50% rate of graft occlusion in 37 patients examined from 2 weeks to 6 months postoperatively.

We believe that the failure of the initial experience with the RA graft was due to the combination of two mechanisms: (1) spasm of the RA conduit and (2) intimal hyperplasia. Spasms of pedicled arterial conduits used for coronary bypass have been recently reported using both the IMA and the gastroepiploic artery [6–8]. Also, it has been shown that spasm may affect free arterial grafts [9]. Our angiographic studies clearly demonstrated the propensity to spasm of the radial artery. This radiologic aspect was noted in 6 patients in the early postoperative angiograms. Spasm was probably induced by the tip of the catheter in at least 3 patients. In the 3 other patients

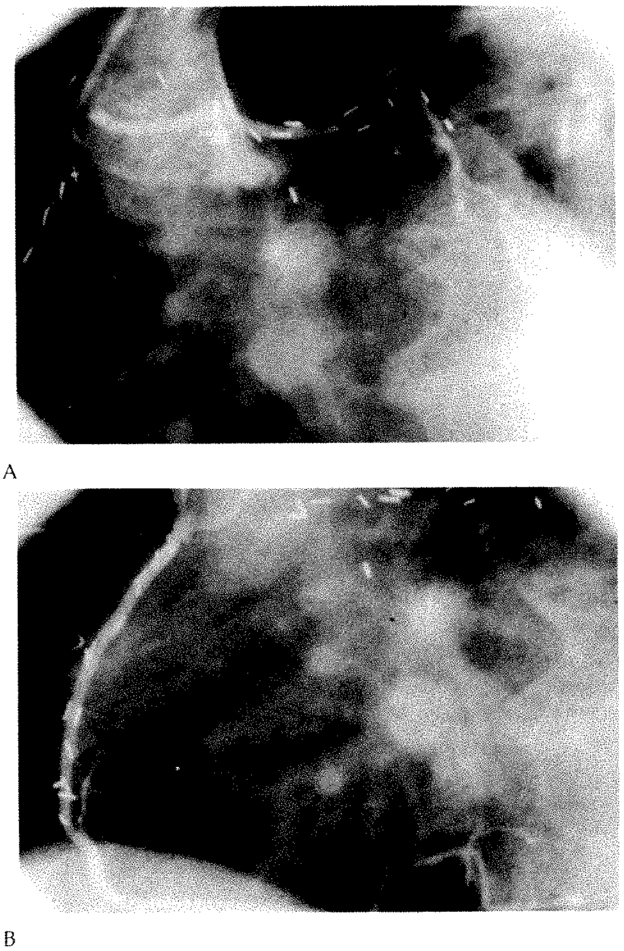


Fig 10. Radial artery grafts to obtuse marginal artery through the transverse sinus (A) and to the right coronary artery (B) at 12 months.

the image displayed was a narrowing involving the graft in two separate segments. These spasms were due to a strong contraction of the arterial wall that could not constantly be released using vasodilators. However, these spasms could be reversible because in at least 2 of our patients they disappeared 6 to 12 months later (see Fig 11). The absence of spasm on the late angiograms suggests that the RA grafts might have lost part of their vascular tone.

The propensity to spasm of the RA is obviously related to the microscopic structure of this vessel. The radial artery is a "muscular" artery with a thick wall whose media contains a high density of leiomyocytes [10]. The RA is very sensitive to mechanical stimuli and reacts instantaneously by producing a spasm. The harvesting technique itself as well as the preparation of the graft used 20 years ago could have been responsible for spasms: the RA was occasionally dissected alone separated from its satellite veins; it was then dilated using metallic probes of increasing size introduced inside the vessel lumen [1]. In the present series the modalities of removal of the radial graft were different: the radial artery was dissected en bloc together with its pedicle; dilation of the graft was then undertaken using blood and papaverine to release any segmental spasms. We believe that this last maneuver is of particular importance, as a spasm present at the time of removal might persist throughout the postoperative period and induce early graft failure. Hydrostatic dilation should be achieved under gentle pressure so as to avoid injury to the internal elastic lamina [11]. No intraluminal instruments were used. All collateral branches, particularly numerous in the RA, were ligated using metallic clips. In addition, spasm was prevented using calcium blockers in this series. All patients received diltiazem starting intravenously at the end of the procedure and continued orally throughout the follow-up period. During coronary angiography, the tip of the angiography catheter as well as the iodic substance injected into the graft may represent a stimulus for spasm of the RA. These spasms may be reversible using in situ vasodilators.

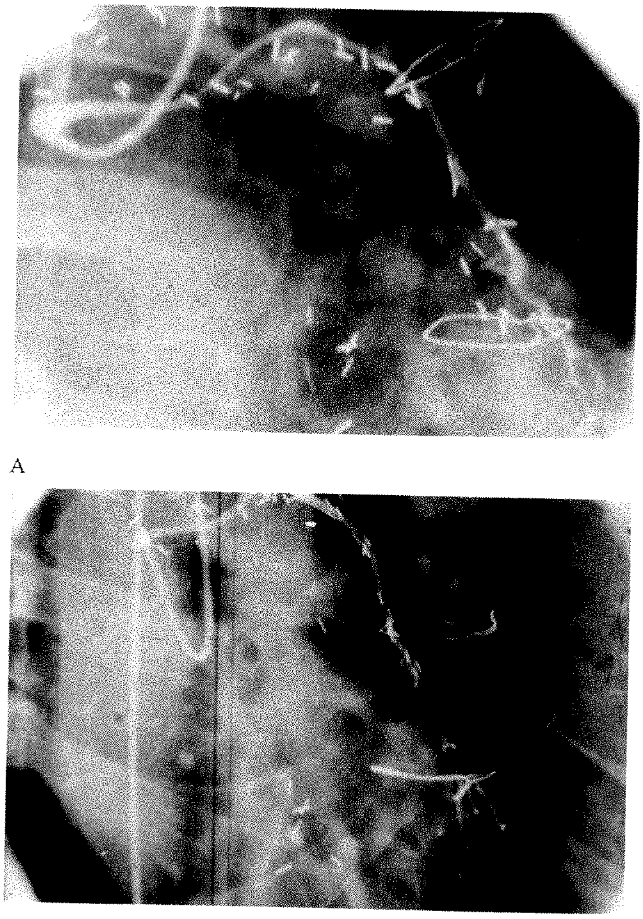


Fig 11. Spasm involving a long portion of a radial artery graft at the postoperative angiogram (A); total release of the spasm 12 months later (B).

Intimal hyperplasia is a mechanism involved in graft failure both in cardiac and vascular operations. It is a nonspecific process that may affect many types of conduit (prosthetic grafts [12, 13], umbilical vein [14], autologous vein [15, 16], and RA [3, 17]). In aging vascular walls the presence of myocytes in the intimal layer is a common finding. However, under certain pathologic conditions, leiomyocytes present in the media would migrate through the fenestrated internal elastic lamina to the intimal layer; the accumulation of leiomyocytes in the intimal layer would then reduce the size of the lumen and progressively lead to vessel occlusion. It is clear that intimal hyperplasia has been involved in the pathogenesis of RA graft failure as shown by microscopic analysis of at least one occluded graft in a patient requiring reoperation [3]. However, we suspect that intimal hyperplasia was a secondary phenomenon induced by injury of the intima during harvesting which resulted in a prolonged spasm causing a reduced and turbulent flow into the graft. The correlation between spasm and intimal hyperplasia has been recently suggested in an experimental model [18].

From a purely surgical standpoint, the radial artery represents an excellent conduit for coronary bypass because (1) it is an arterial graft used to systemic pressure regimen, (2) its diameter, slightly greater than the IMA, corresponds perfectly to the diameter of most coronary arteries, (3) the quality of its wall (thick and resistant) offers very good technical conditions for coronary and aortic anastomosis, and (4) its length (usually more than 20 cm) allows it to reach all target vessels on the surface of the heart. Moreover, in some instances two distinct graftings can be performed using two segments of the same radial artery.

A point of concern when planning to use the RA is the potential deleterious effect on the vascular supply of the forearm and the hand. The forearm and the hand are mainly vascularized by the ulnar artery and its collateral branches [19, 20]. Although anatomic variations of the RA are not exceptional, the ulnar artery always supplies the radial artery territory through distal anastomosis. The Allen test has been suggested to detect patients in whom collateral flow from the ulnar artery is insufficient in case of radial artery occlusion. Although this test has been criticized in the literature for frequent false positives [21], it is a simple maneuver that we routinely perform before RA removal. More important are Doppler studies, which can detect any abnormality of vascular distribution of the upper limb. Up to now, no patient has been contraindicated for RA removal, and no ischemic event of the upper limb was observed in this series.

No local complications were observed after RA harvesting. However, transitory dysesthesia of the thumb with no functional disturbance, probably due to surgical trauma of the superficial branch of the radial nerve, was noted in 8 patients. Like most arteries of the upper limb, the RA is very rarely affected by atherosclerosis. Although 20% of our patients had multiple sites of atherosclerotic disease, with prior vascular surgical procedures in 15 patients, the RA was always macroscopically normal. However, 1 severely diabetic patient had localized calcifications of the RA at the pulse groove; the proximal segment of this artery was used with a good early result.

In conclusion, pedicled IMA continues to be the graft of choice in coronary artery revascularization. The need for total revascularization raises the problem of which other conduits should be used to complement the IMA. This report shows encouraging early patency rates of the RA when properly used with vasodilators. However, a randomized study including a large number of patients with late control angiograms is yet required to establish the place of this graft in coronary artery bypass grafting.

References

1. Carpentier A, Guermonprez JL, Deloche A, Frechette C, Dubost C. The aorta-to-coronary radial artery bypass graft: a technique avoiding pathological changes in grafts. Ann Thorac Surg 1973;16:111–21.
2. Carpentier A. Discussion of Geha AS, Krone RJ, McCormick JR, Baue AE. Selection of coronary bypass: anatomic, physiological, and angiographic considerations of vein and mammary artery grafts. J Thorac Cardiovasc Surg 1975;70:414–31.
3. Curtis JJ, Stoney WS, Alford WC, Burrus GR, Thomas CS. Intimal hyperplasia: a cause of radial artery aortocoronary bypass graft failure. Ann Thorac Surg 1975;20:628–35.
4. Dion R, Etienne PY, Verhelst R, Baele P, Wyns W, Chalant C. The right mammary artery as coronary bypass graft: techniques and results in 200 consecutive patients [Abstract]. J Cardiovasc Surg 1991;32:71.
5. Fisk RL, Brooks CH, Callaghan JC, Dvorkin J. Experience with the radial artery graft for coronary bypass. Ann Thorac Surg 1976;21:513–8.
6. Sarabu MR, McClung JA, Fass A, Reed GE. Early postoperative spasm in left internal mammary artery bypass grafts. Ann Thorac Surg 1987;44:199–200.
7. Blanche C, Chaux A. Spasm in mammary artery grafts [Letter]. Ann Thorac Surg 1988;45:586.
8. Suma H. Spasm of the gastroepiploic artery graft. Ann Thorac Surg 1990;49:168–9.
9. Mills NL, Everson CT. Right gastroepiploic artery: a third arterial conduit for coronary artery bypass. Ann Thorac Surg 1989;47:706–11.
10. Van Son JA, Smedts F, Vincent JG, Van Lier HJ, Kubat K. Comparative anatomic studies of various arterial conduits for myocardial revascularization. J Thorac Cardiovasc Surg 1990; 99:703–7.
11. Sims FH. Discontinuities in the internal elastic lamina: a comparison of coronary and internal mammary arteries. Artery 1985;13:127–43.
12. Green RM, Thomas M, Luka N, De Weese JA. A comparison of rapid healing prosthetic arterial grafts and autogenous veins. Arch Surg 1979;114:944.
13. Echave V, Kcornick AR, Haimov M, Jacobson JH. Intimal hyperplasia as a complication of the use of the polytetrafluoroethylene graft for femoral-popliteal bypass. Surgery 1979; 86:791.
14. Dardick H, Baier RE, Weinberg S, et al. Morphologic and biophysical assessment of long term human umbilical cord vein implants used as vascular conduits. Surg Gynecol Obstet 1982;154:17.
15. Johnson WD, Avery JE, Tector AJ. Late changes in coronary vein grafts. Am J Cardiol 1970;26:640.
16. Grondin CM, Meere C, Castonguay Y, Lepage G, Grondin P. Progressive and late obstruction of an aorta-coronary venous bypass graft. Circulation 1971;43:698.
17. Chiu R-CJ. Why do radial artery grafts for aortocoronary bypass fail? A reappraisal. Ann Thorac Surg 1976;22:520–3.
18. Massa G, Johansson S, Kimblad PO, Sjoberg T, Steen S. Might free arterial grafts fail due to spasm? Ann Thorac Surg 1991;5:94–101.
19. Lippert H, Pabst RA. Arteries of the forearm. In: Bergmann JF, ed. Arterial variations in man: classification and frequency. Verlag Munchen, 1985:71–7.
20. Hoeber PB. Vessels and nerves of the flexor forearm. In: Hoeber PB, ed. Anatomy for surgeons: the back and limbs. Harper & Brothers, 1958:413–9.
21. Kaminski RW, Barnes RW. Critique of the Allen test for continuity of the palmar arch assessed by Doppler ultrasound. Surg Gynecol Obstet 1976;142:861–4.

DISCUSSION

DR WILLIAM A. COLTHARP (Nashville, TN): I congratulate Dr Acar and his colleagues on this excellent presentation of their experience with the radial artery graft. The results obtained using the vasoactive drugs to combat the arterial spasm are impressive. I would like to contrast these results with those obtained by my associates in Nashville with our previously reported early follow-up of radial artery grafts and provide long term follow-up data on these same patients.

In 1974, my associates published in *The Annals of Thoracic Surgery* a series of 29 patients who received radial artery grafts for coronary bypass; 34 radial artery grafts were used in those 29 patients, and the follow-up was recatheterization 1 week to 1 year after the operation. At that early follow-up, 33% of the radial artery grafts were occluded.

We have recently reviewed long-term follow-up data in those same 79 patients. Fifty-three of them have since been restudied with a total of 61 radial artery grafts, again, 7 days to 16.3 years after the operation. At that restudy time 51% of the grafts were occluded.

Assuming that the radial artery grafts were patent until proven occluded and using an occluded radial artery graft as a death of the graft, we constructed a Kaplan-Meier life-table or survival curve for the radial artery grafts based on our experience. At 5 years, or about 1,800 days, the patency rate of the radial artery grafts is about 65%. The initial fall in patency rate we attributed to intimal hyperplasia. At 10 years, or about 3,600 days, the patency rate is still 60% and the grafts that were allotted 5 years have a reasonable lifespan expectancy.

I would like to make two points regarding our results. The first is that we also think that intimal hyperplasia is the culprit for graft occlusion of the radial artery graft. We have attributed this to the vigorous manual dilation that was used to combat the arterial spasm in this series of patients. Combating the spasm with vasoactive drugs as Dr Acar and his associates recommend is a logical step, and in their hands seems to eliminate this early intimal hyperplasia leading to graft closure.

The second point is a word of caution regarding hand claudication. We have seen hand claudication in 2 patients after radial artery harvesting. One of those was a dentist who suffered major disability after that claudication. In fact, that patient was important in our decision to stop using the radial artery graft. On the day before operating on a prominent general surgeon in Nashville, Dr Stoney, pondering the consequences of claudication and intimal hyperplasia, phoned Dr Carpentier to discuss his results and opinions on the radial artery graft. They both agreed at that time that it was not an optimal conduit, and no more have been used at St. Thomas Hospital.

Perhaps the present study and the recommended techniques for combating arterial spasm will bring us full circle to where once again the radial artery is recommended as a bypass conduit.

DR ACAR: I thank Dr Coltharp for his comments. In 1975, 2 years after having performed the first coronary bypass using the radial artery graft, Professor Carpentier at the meeting of the American Association for Thoracic Surgery in New York reported angiographic results similar to those you showed with a 35% incidence of narrowing or occlusion of the radial artery. He therefore recommended that the use of this graft should be discontinued.

He suggested that the etiopathology of this occlusion was a spasm of the radial artery. Twenty years later, our study supports this hypothesis. Early control showed a 10% incidence of spasm of the radial artery and 0% of early occlusion, which compares favorably with the 35% early occlusion in the 1975 series. This difference is probably due to the systemic use of calcium blockers, a drug that was not available at that time.

The radial artery is very sensitive to mechanical stimuli, as we saw in the operation room. At the time of removal it is particularly important to avoid any trauma that could induce a spasm persistent throughout the operation, thus leading to secondary graft failure. We now harvest the artery together with its satellite veins, a precaution that was not systematically taken in the past.

In addition, mechanical dilation of the radial artery graft is not used any more. Instead, hydrostatic dilation of the graft is undertaken using blood and papaverine. The exact place of the radial artery compared with other types of conduits will be defined in the future on a large number of controlled angiograms. We believe that the internal mammary artery is the best arterial conduit. However, the question remains which is the best arterial conduit to complement the internal mammary artery.

With regard to possible detrimental effects on the vascularization of the hand after radial artery removal, we have not observed any claudication of the upper limb in our series.

DR ALAIN F. CARPENTIER (Paris, France): It is interesting to see that a better understanding of the pathogenesis of arterial spasm as well as new drugs have changed our view on a conduit that we condemned 20 years earlier.

To answer the question on our current policy in using the radial artery today in my service, our first choice as an arterial conduit remains of course the pedicled mammary artery. The second choice is the radial artery, which has been superior in our experience to free mammary artery and infraepigastric artery.

Clinical and Hemodynamic Assessment of the Hancock II Bioprosthesis

Tirone E. David, MD, Susan Armstrong, MSc, and Zhao Sun, MA

Division of Cardiovascular Surgery, The Toronto Hospital and University of Toronto, Toronto, Ontario, Canada

The Hancock II bioprosthesis was used for heart valve replacement in 614 patients from 1982 to 1990. Aortic valve replacement (AVR) was performed in 376 patients, mitral valve replacement (MVR) in 195, and aortic and mitral valve replacement (DVR) in 43. The mean age was 62.7 years, and 78% of all patients were in New York Heart Association functional class III or IV before operation. Coronary artery bypass graft was necessary in 232 patients and replacement of ascending aorta in 55. There were 31 operative deaths (AVR, 4%; MVR, 6%; DVR, 9%). Follow-up was complete in 98.5% of the patients and extended from 12 to 103 months, with a mean of 49 months. At the last follow-up, 85% of the patients were in New York Heart Association class I or II. The actuarial survival at 8 years was 79% ± 3% for AVR, 68% ± 4% for MVR, and 65% ± 10% for DVR. The freedom from stroke at 8 years was 93% ± 2% for AVR, 83% ± 5% for MVR, and 90% ± 5% for DVR. At the end of 8 years 96% ± 1% of all patients were free from endocarditis, 92% ± 1% were free from primary tissue failure, and 89% ± 3% were free from reoperation. The actuarial freedom from valve-related death at 8 years was 98% ± 1% for AVR, 86% ± 5% for MVR, and 91% ± 6% for DVR. Hemodynamic assessment was obtained by Doppler echocardiography in all operative survivors and demonstrated satisfactorily effective valve orifices and transvalvular gradients. The clinical results obtained with the Hancock II bioprosthesis have been gratifying, particularly in the aortic position. This bioprosthesis is our biological valve of choice.

(Ann Thorac Surg 1992;54:661–8)

The Hancock II bioprosthesis differs from its predecessors in the following aspects: the porcine aortic valve is fixed with a buffered solution of 0.625% glutaraldehyde in two stages, an initial stage of low pressure and a late stage of physiologic pressure; the stent is made of Delrin; and the tissue is treated with sodium dodecyl-sulfate to retard calcification [1]. The Hancock II bioprosthesis used for aortic valve replacement is designed to be implanted in a supraannular position. The first Hancock II bioprosthesis was implanted at The Toronto Hospital in September 1982. This article is a review of all patients who received this bioprosthesis at that hospital.

Patients and Methods

From September 1982 to May 1990, the Hancock II bioprosthesis was used for heart valve replacement in 614 patients: 397 men and 217 women. The mean age of the patients was 62.7 years and ranged from 18 to 86 years. Patients were divided into three groups: 376 patients had the aortic valve replaced with a Hancock II bioprosthesis (AVR), 195 had the mitral valve replaced (MVR), and 43 had both the aortic and mitral valve replaced (DVR). The clinical profiles of these patients are summarized in Table 1. Patients who had one valve repaired and one replaced with a Hancock II bioprosthesis were included under single valve replacement. Three patients had tricuspid valve replacement and were included in one of the above groups. One patient had aortic, pulmonary, and tricuspid valve replacement and was included in the AVR group.

The operative procedures performed on these patients are listed in Table 2. The left atrial appendage orifice was oversewn from inside the left atrium in patients who had MVR. An effort was always made to match the size of the bioprosthesis to the body surface area of the patient to minimize transvalvular gradients. The guidelines for this matching were developed early in our experience with this bioprosthesis and are shown in Table 3.

All operative survivors were discharged from the hospital on a regimen of warfarin sodium and were instructed to discontinue it after 3 months. After 1984 all patients were told to take 325 mg of aspirin a day after discontinuing warfarin administration.

Operative survivors were followed up from October 1982 to September 1991. With the exception of 9 patients (1.5%) who were lost to follow-up, all survivors were contacted by telephone or questionnaire in 1991. The mean follow-up was 49 ± 24 months (range, 12 to 103 months). Of the 9 patients lost to follow-up, 5 had had AVR, 3 MVR, and 1 DVR.

Postoperative complications were prospectively compiled and analyzed according to the "Guidelines for reporting morbidity and mortality after cardiac valvular operations" approved by The Society of Thoracic Surgeons [2]. The cause of death was established from information obtained from hospital or attending physician's records or autopsy reports. Bioprosthetic valve failure was defined as any clinically significant valve

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr David, 200 Elizabeth St, 13EN219, Toronto, Ont M5G 2C4, Canada.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Clinical Profile of the Patients[a]

Variable	AVR	MVR	DVR
No. of patients	376	195	43
Age (years, mean ± standard deviation)	63 ± 12	63 ± 11	60 ± 12
Sex			
Male	279 (74)	89 (46)	29 (67)
Female	97 (26)	106 (54)	14 (33)
ECG			
Sinus rhythm	334 (89)	91 (47)	21 (49)
Atrial fibrillation	33 (9)	93 (48)	18 (48)
Heart block	9 (2)	11 (5)	4 (9)
NYHA functional classification			
I	9 (2)	2 (1)	1 (2)
II	103 (27)	14 (7)	6 (14)
III	143 (38)	79 (40)	9 (20)
IV	121 (32)	100 (51)	27 (63)
Previous valve operation			
AVR/repair	17 (4)	2 (1)	11 (26)
MVR/repair	0	39 (20)	11 (26)
TV repair	0	1 (0.5)	1 (2)
Active infective endocarditis	14 (4)	11 (6)	6 (14)
Aortic valve lesion			
Stenosis	160 (42)	. . .	8 (19)
Insufficiency	100 (27)	. . .	20 (46)
Mixed	116 (31)	. . .	15 (35)
Mitral valve lesion			
Stenosis	2 (0.5)	42 (21)	11 (25)
Insufficiency	25 (7)	109 (56)	17 (39)
Mixed	3 (0.8)	44 (22)	15 (34)
Tricuspid valve lesion			
Stenosis	0	3 (2)	1 (2)
Insufficiency	0	29 (15)	7 (16)
Coronary artery disease			
None	226 (60)	108 (55)	28 (65)
One-vessel	44 (12)	27 (14)	7 (16)
Two-vessel	56 (15)	20 (10)	5 (11)
Three-vessel	50 (13)	40 (20)	3 (7)
Left ventricular ejection fraction			
>0.54	53 (14)	61 (31)	3 (7)
0.40–0.54	117 (31)	70 (36)	11 (25)
0.20–0.40	60 (16)	35 (18)	15 (35)
<0.20	28 (8)	12 (6)	2 (5)
Undetermined	118 (30)	17 (9)	12 (28)

[a] Values in parentheses are percentages.

AVR = aortic valve replacement; DVR = aortic and mitral valve replacement; ECG = electrocardiogram; MVR = mitral valve replacement; NYHA = New York Heart Association; TV = tricuspid valve.

Table 2. Operative Data[a]

Variable	AVR	MVR	DVR
Aortic valve replacement	376	0	43
Mitral valve replacement	0	195	43
Tricuspid valve replacement	1	1	1
Pulmonary valve replacement	1	0	0
Mitral valve repair	30 (8)	0	0
Tricuspid valve repair	0	31 (16)	7 (16)
Replacement of the ascending aorta	49 (13)	2	4
Patch enlargement of aortic root	79 (21)	0	6
Reconstruction of the mitral annulus	0	7	2
Coronary artery bypass	143 (38)	75 (38)	17 (39)
Repair of LV aneurysm	4	6	0
Abdominal aortic aneurysm repair	5	3	0
Size of aortic bioprosthesis			
21 mm	22 (6)	0	5 (12)
23 mm	81 (21)	0	7 (16)
25 mm	105 (28)	0	15 (35)
27 mm	133 (35)	0	12 (28)
29 mm	35 (9)	0	4 (9)
Size of mitral bioprosthesis			
27 mm	0	16 (8)	3 (7)
29 mm	0	64 (33)	4 (9)
31 mm	0	90 (46)	26 (60)
33 mm	0	25 (13)	10 (23)

[a] Values in parentheses are percentages.

AVR = aortic valve replacement; DVR = aortic and mitral valve replacement; LV = left ventricular; MVR = mitral valve replacement.

stenosis or insufficiency documented by Doppler echocardiography, reoperation, or autopsy.

All operative survivors had at least one echocardiographic study during the first year after the operation and whenever they experienced a cardiac or valvular complication.

Statistical analyses were performed with SAS (Statistical Analysis System Institute Incorporated, Cary, NC) and BMDP (BMDP Statistical Software, Los Angeles, CA) software. Postoperative events were characterized by actuarial statistics with the Kaplan-Meier method [3]. Results were expressed in percentages of the means and percentages of the standard errors of the means. Fisher's exact test or contingency table analysis was used to compare the thromboembolic rates in certain subgroups of patients.

Results

Patient Survival

The operative mortality and morbidity are shown in Table 4. There were 31 operative and 74 late deaths. The causes of late deaths are listed in Table 5.

Table 3. Guidelines for Matching Size of Bioprosthesis With Patient's Size

BSA (m^2)	Aortic Valve (mm)	Mitral Valve (mm)
<1.60	21 or larger	27 or larger
<1.70	23 or larger	27 or larger
<1.80	25 or larger	29 or larger
>1.80	27 or larger	31 or larger

BSA = body surface area.

Table 4. Operative Mortality and Morbidity

Variable	AVR	MVR	DVR
Operative mortality	15 (4%)	12 (6%)	4 (9%)
Causes of death			
Myocardial infarction	4	3	1
Low cardiac output syndrome	6	7	2
Stroke	2	1	0
Multiple organ failure	3	1	1
Operative morbidity			
Reexploration for bleeding	29	13	2
Reexploration for cardiac arrest	2	1	1
Low cardiac output syndrome	34	38	12
Perioperative myocardial infarction	8	6	2
Perioperative stroke or TIA	9	9	0
Sternal infection	0	0	0
Permanent pacemaker	19	16	8

AVR = aortic valve replacement; DVR = aortic and mitral valve replacement; MVR = mitral valve replacement; TIA = transient ischemic attack.

Figure 1 shows the actuarial survival for patients who had AVR, MVR, and DVR. The survival at 8 years was 79% ± 3% for AVR, 64% ± 5% for MVR, and 64% ± 11% for DVR.

The actuarial freedom from cardiac and valve-related deaths at 5 and 8 years is shown in Table 6.

Anticoagulant and Thromboembolic Complications

There were no hemorrhagic complications during the first 3 postoperative months while all operative survivors were receiving warfarin sodium. A number of patients continued to take oral anticoagulant beyond the third month, and 3 patients suffered serious hemorrhagic complications with the resulting death of 1. At the last follow-up, 98 patients (28 AVR, 57 MVR, and 13 DVR) were taking warfarin, 312 patients (228 AVR, 69 MVR, and 15 DVR) were taking aspirin, and 84 patients were not taking either warfarin or aspirin. There were no cases of bioprosthetic valve thrombosis.

There were 23 thromboembolic events in the AVR group: eight strokes (one was fatal) and 15 transient cerebral ischemic attacks. The anticoagulant status of these patients at the time of the thromboembolic event was as follows: 7 patients were not taking any drugs, 6 were taking warfarin, and 7 were taking aspirin. Patients taking aspirin had a significantly lower thromboembolic risk than those taking warfarin or no medication ($p < 0.01$). Patients who had AVR and coronary artery bypass had a higher incidence of thromboembolic complications than those who had isolated AVR ($p < 0.02$). Patients who had associated operations such as mitral valve repair (30 patients) or replacement of the ascending aorta (49 patients) had the same risk of thromboembolic complication as patients who had only AVR. The actuarial freedom from thromboembolic events in patients who had AVR is shown in Figure 2. At 8 years, 80% ± 5% of the patients had not had any thromboembolic complication and 93% ± 2% had not had strokes.

Table 5. Causes of Late Deaths

Cause	AVR	MVR	DVR
Valve-related			
Stroke	1	6	0
Endocarditis	2	2	2
Anticoagulant-related hemorrhage	0	1	0
Valve dehiscence	0	1	0
Cardiac			
Myocardial infarction/sudden death	9	3	1
Congestive heart failure	7	10	0
Noncardiac	15	10	3
Unknown	0	1	0

AVR = aortic valve replacement; DVR = aortic and mitral valve replacement; MVR = mitral valve replacement.

Table 6. Freedom From Cardiac and Valve-Related Death

Event	AVR	MVR	DVR
Freedom from cardiac death			
At 5 years	90% ± 2%	81% ± 3%	86% ± 6%
At 8 years	86% ± 3%	74% ± 5%	86% ± 6%
Freedom from valve-related death			
At 5 years	99% ± 0.6%	94% ± 2%	91% ± 6%
At 8 years	98% ± 1%	86% ± 5%	91% ± 6%

AVR = aortic valve replacement; DVR = aortic and mitral valve replacement; MVR = mitral valve replacement.

There were 19 thromboembolic events in the MVR group: 14 strokes (six were fatal) and five transient cerebral ischemic attacks. The anticoagulation regimen of these patients at the time of the thromboembolic event was the following: 7 patients were taking warfarin, 6 were taking aspirin, and 6 had no anticoagulants. Chronic atrial fibrillation was not associated with a higher incidence of thromboembolic events, but all patients in atrial fibrillation were taking either aspirin or warfarin. The actuarial freedom from thromboembolic complications in patients who had MVR is shown in Figure 3. At 8 years, 74% ± 7% of the patients had not had any thromboembolic event and 83% ± 5% had not had strokes.

Patients who had MVR had a higher rate of strokes than patients who had AVR ($p < 0.05$), but the overall rates of thromboembolic complications in patients who had AVR and MVR were not significantly different.

In the DVR group, 3 patients suffered a stroke. The actuarial freedom from thromboembolic complications in patients who had DVR was 90% ± 5% at 8 years.

Bioprosthetic Valve Endocarditis

Twelve patients had bioprosthetic valve endocarditis (4 AVR, 5 MVR, and 3 DVR). Four patients were treated with antibiotics and operation: 3 survived and 1 died. Eight patients were treated with antibiotics alone: 3 survived and 5 died. The actuarial freedom from bioprosthetic valve endocarditis for all patients at 5 and 8 years

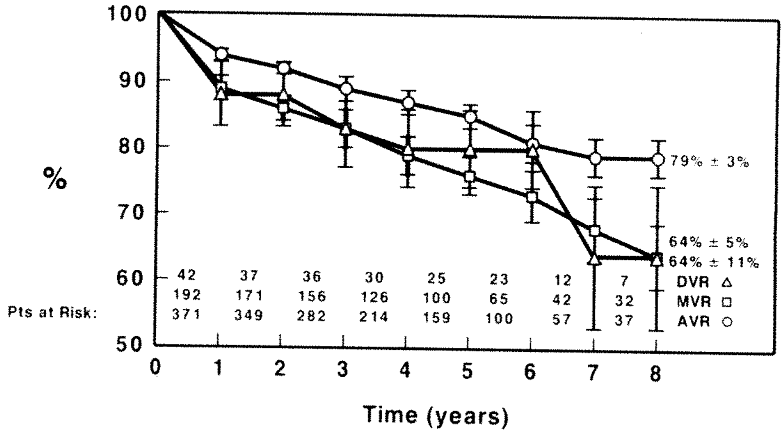


Fig 1. Actuarial survival curves in patients who had aortic valve replacement (AVR), mitral valve replacement (MVR), and both aortic and mitral valve replacement (DVR).

was 97% ± 1% and 96% ± 1%, respectively. The actuarial freedom from bioprosthetic valve endocarditis in patients who had AVR, MVR, and DVR is shown in Figure 4.

Bioprosthetic Valve Failure

Six patients experienced bioprosthetic valve incompetence because of primary tissue failure in 5 (3 AVR, 1 MVR, and 1 DVR) and tissue overgrowth on one of the leaflets with resulting mitral incompetence in 1. All 6 patients were successfully reoperated on. The five valves that failed because of primary tissue failure displayed tears in one or more leaflets in the commissural areas, and only mild calcification.

The actuarial freedom from primary tissue failure for all patients at 5 and 8 years was 99% ± 0.4% and 92% ± 3%, respectively. The actuarial freedom from primary tissue failure in patients who had AVR, MVR, and DVR is shown in Figure 5.

Reoperations

Fifteen patients underwent reoperation: 7 in the AVR group, 4 in the MVR group, and 4 in the DVR group. The indications for reoperation were bioprosthetic valve failure in 6 patients, endocarditis in 4, progression of coronary artery disease in 2, progression of mitral valve disease in a patient who had AVR, paravalvular leak in 1, and acute aortic dissection in 1. The bioprosthetic valve was explanted in 2 of the latter 5 patients because it had been in for more than 5 years though it was still functioning normally. There was only one death among these 15 patients reoperated on; it occurred after endocarditis and septic shock developed in a patient who had had DVR.

The actuarial freedom from reoperation in all patients at 5 and 8 years was 97% ± 1% and 89% ± 3%, respectively. The actuarial freedom from reoperation in patients who had AVR, MVR, and DVR is shown in Figure 6.

Hemodynamic Assessment

Although 574 operative survivors had a Doppler echocardiographic study performed during the first year after the operation, only 152 had the study done at our institution and following the same protocol. These 152 studies formed the base for the hemodynamic assessment of the Hancock II bioprosthesis. The hemodynamic data obtained by Doppler echocardiography are shown in Table 7. Paravalvular leak was detected in only 1 patient who had AVR and was reoperated on.

Late Functional Classification

At the last follow-up, 491 patients were alive and had their original Hancock II bioprosthesis: 318 AVR, 143 MVR, and 30 DVR. Of the patients who had AVR, 197 (62%) were in New York Heart Association functional class I, 87 (27%) in class II, and 34 (11%) in class III. Of the patients who had MVR, 74 (54%) were in functional class I, 38 (26%) in class II, 30 (21%) in class III, and 1 in class

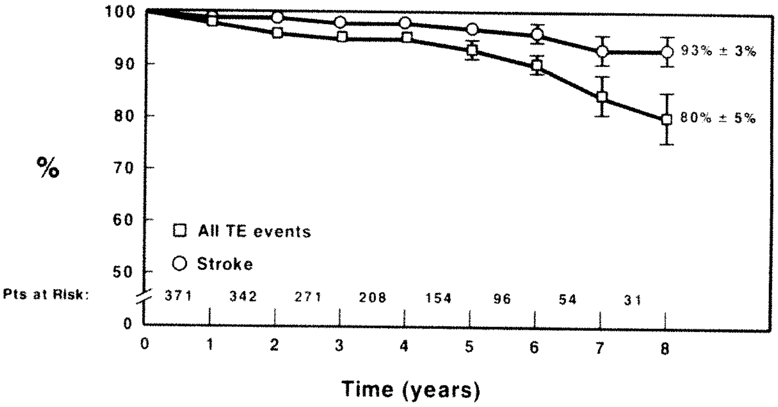


Fig 2. Actuarial freedom from thromboembolic (TE) complications in patients who had aortic valve replacement.

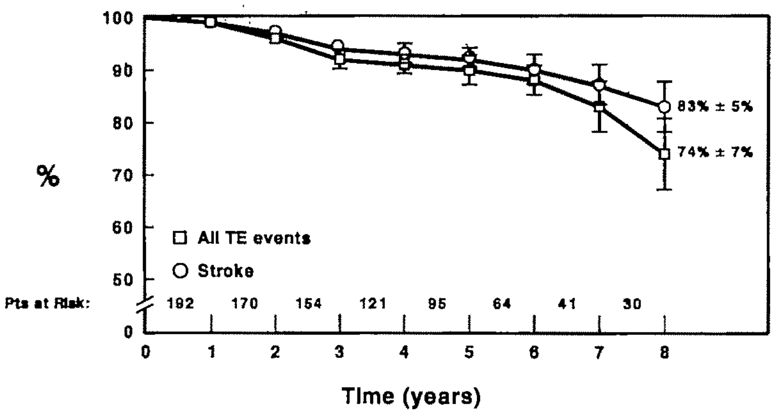


Fig 3. Actuarial freedom from thromboembolic (TE) complications in patients who had mitral valve replacement.

IV. Of the patients who had DVR, 8 (27%) were in class I, 16 (53%) in class II, 5 (17%) in class III, and 1 in class IV. Of the 72 patients who were in New York Heart Association class III or IV, 11 were disabled because of angina pectoris and 61 because of shortness of breath or fatigue despite satisfactory bioprosthetic valve function as assessed by echocardiography.

Comment

The Hancock bioprosthesis became commercially available in 1970. The porcine aortic valve was fixed in a closed position at near-physiologic pressure with a stabilized solution of glutaraldehyde, and it was mounted in a Dacron cloth-covered rigid metal stent [4]. To reduce the mechanical stress on the leaflets during closure of the valve, a flexible polypropylene stent was developed and replaced the rigid metal stent in 1971 [5]. As clinical experience with this bioprosthesis increased, certain problems became apparent and modifications were made to improve its performance. Its obstructive nature was largely due to the physical properties of the fixed tissue, the stent, and the muscle bar to which the right cusp is attached. This problem was partially resolved by better tissue selection and further improved by excising the right cusp and replacing it with a larger noncoronary cusp of another valve. This resulting composite valve is referred to as the Hancock modified orifice valve and was introduced for clinical use in 1977. Although the clinical performance of the Hancock modified orifice valve appears to be similar to that of the standard Hancock valve, its effective orifice is larger [6, 7].

Porcine bioprostheses have a limited durability because of tissue degeneration. Mechanical stress and host reactions to the porcine valve are the main causes of tissue degeneration. It has been shown that the pressure that the leaflets are exposed to during fixation with glutaraldehyde affects their dynamic features as well as their resistance to fatigue [8]. Calcification of the leaflets is also part of the degenerative process, and it is possible to decrease mineralization of the porcine valve leaflets by treating them with certain calcium-mitigating agents [9, 10]. Finally, the stent also plays a role in the mechanical stress that the leaflets are subjected to during the cardiac cycle [5]. These factors were incorporated in the development of the Hancock II bioprosthesis in an attempt to improve its hemodynamic performance and durability. The Hancock II bioprosthesis has not been available long enough to determine whether it is more durable than other porcine valves, but by comparing our results with those reported by other investigators on the standard Hancock valve and the standard and supraannular Carpentier-Edwards bioprostheses [11–17], we found a lower rate of bioprosthetic valve failure at 8 years. However, the differences may be explained by other factors that affect the durability of bioprostheses such as the age of the

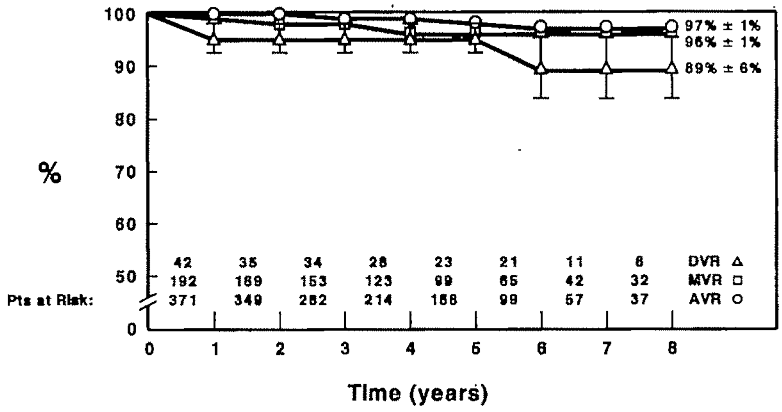


Fig 4. Actuarial freedom from bioprosthetic endocarditis in patients who had aortic valve replacement (AVR), mitral valve replacement (MVR), and both aortic and mitral valve replacement (DVR).

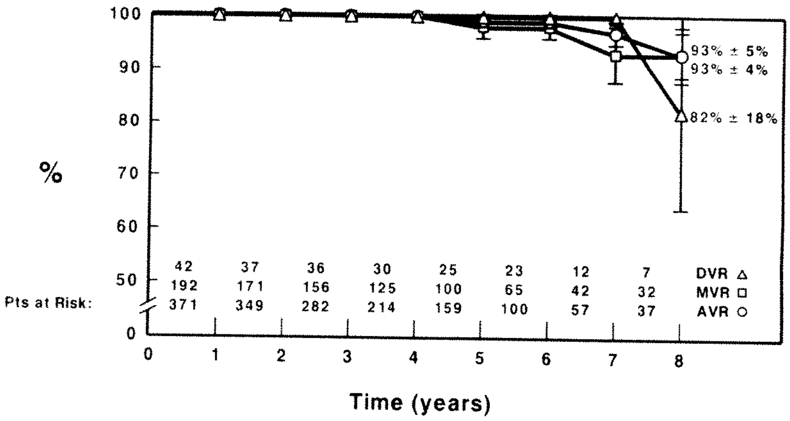


Fig 5. Actuarial freedom from bioprosthetic valve failure in patients who had aortic valve replacement (AVR), mitral valve replacement (MVR), and both aortic and mitral valve replacement (DVR).

patients. Our patients were older than in other reported series [11–13].

Although many factors affect the long-term survival of patients after heart valve replacement, an actuarial survival of 79% at 8 years after AVR is excellent, particularly because the mean age of our patients was 63 years and more than one-third of them had coronary artery disease. This high survival in our patients is partly due to the freedom from valve-related deaths among patients who had AVR. The actuarial survival in patients who had MVR or DVR was similar to those reported for other porcine bioprostheses [11–17].

The rate of thromboembolic complications observed in our patients was higher than that reported for other bioprostheses [11–17]. The difference lies largely in the number of transient cerebral ischemic attacks. We believe that high thromboembolic incidence is not a problem associated with the Hancock II bioprosthesis but is rather due to our interpretation of the patients' symptoms, as we found similar rates with other bioprostheses [18]. Most thromboembolic events in patients who had AVR were transient cerebral ischemic attacks, whereas most events in patients who had MVR were completed strokes. The freedom from all thromboembolic events at 8 years was 80% for AVR and 75% for MVR, whereas the freedom from stroke was 93% for AVR and 83% for MVR. Patients who were receiving aspirin had a lower thromboembolic rate, particularly if they had had AVR. Patients who had isolated AVR were found to have a lower thromboembolic rate than those who had AVR and coronary artery bypass.

The risk of endocarditis in patients with the Hancock II bioprosthesis is similar to that reported for other bioprostheses [11–17]. The freedom from endocarditis at 8 years was 96% for all patients.

Echocardiographic assessment of the Hancock II bioprosthesis revealed that its effective orifice is satisfactory and compares favorably with that of other porcine bioprostheses [19, 20]. It is important to match the size of the patient to the size of the bioprosthesis as shown in Tables 3 and 7. Small valves should be implanted in small patients. This is the reason why we had to enlarge the aortic root of 79 patients (21%) who had AVR.

Patients must be matched not only to the correct size of heart valve prosthesis but also to the type. The decision as to whether to use a biological or a mechanical heart valve can usually be made before the operation, and the patient, the primary physician, and the attending cardiologist should be part of the decision-making. Valve replacement with a porcine bioprosthesis offers a great opportunity to restore the patient's health and normal life-style, particularly in older patients who need AVR. However, there may be no advantage in using a porcine valve in patients

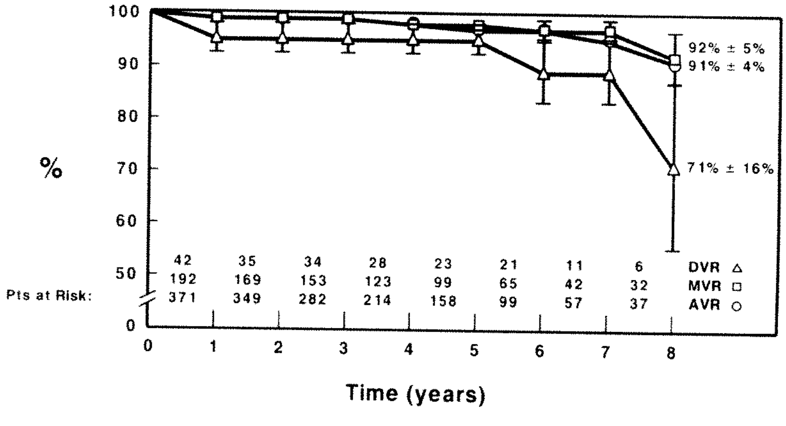


Fig 6. Actuarial freedom from reoperation in patients who had aortic valve replacement (AVR), mitral valve replacement (MVR), and both aortic and mitral valve replacement (DVR).

Table 7. Results of Hemodynamic Assessment of the Hancock II Bioprosthesis by Doppler Echocardiography[a]

	Aortic Bioprosthesis					Mitral Bioprosthesis			
Variable	21	23	25	27	29	27	29	31	33
Body surface area (m^2)	1.55	1.63	1.76	1.91	1.94	1.48	1.68	1.82	1.85
	(0.09)	(0.08)	(0.10)	(0.07)	(0.07)	(0.10)	(0.11)	(0.09)	(0.08)
Peak systolic gradient (mm Hg)	20	23	20	14	15				
	(4)	(3)	(2)	(3)	(3)				
Valve area (cm^2)	1.18	1.33	1.46	1.55	1.60	2.21	2.77	2.84	3.15
	(0.11)	(0.16)	(0.15)	(0.18)	(0.15)	(0.14)	(0.11)	(0.10)	(0.22)

[a] Values are expressed as mean; standard deviation is shown in parentheses.

who need MVR because of the high incidence of atrial fibrillation and consequent need for permanent anticoagulation.

This study was supported by a grant from the Heart and Stroke Foundation of Ontario.

We are indebted to Dr A. Kerwin and Ms J. David for their assistance in the preparation of the manuscript.

References

1. Wright JTM, Eberhardt CE, Gibbs ML, Saul M, Gilpin CB. Hancock II—an improved bioprosthesis. In: Cohn LH, Gallucci V, eds. Cardiac bioprostheses. New York: Yorke Medical, 1982:425.
2. Edmunds LH Jr, Clark RE, Cohn LH, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ann Thorac Surg 1988;46:257–9.
3. Kaplan EL, Meier O. Non-parametric estimations from incomplete observations. J Am Stat Assoc 1958;53:457–81.
4. Kaiser GA, Hancock WD, Lukban SB, Litwak RS. Clinical use of a new design stented xenograft heart valve prosthesis. Surg Forum 1969;20:137–8.
5. Reis RL, Hancock WD, Yarbrough JW, Glancy DL, Morrow AG. The flexible stent. A new concept in the fabrication of tissue heart valve prostheses. J Thorac Cardiovasc Surg 1971;62:683–9.
6. Cohn LH, DiSesa VJ, Collins JJ Jr. The Hancock modified-orifice porcine bioprosthetic valve: 1976–1988. Ann Thorac Surg 1989;48:S81–2.
7. Zusman DR, Levine FH, Carter JE, Buckley MJ. Hemodynamic and clinical evaluation of the Hancock modified orifice aortic bioprosthesis. Circulation 1981;64(Suppl 2):189–91.
8. Broom ND, Thomson FJ. Influence of fixation conditions on the performance of glutaraldehyde-treated porcine aortic valves. Towards a more scientific basis. Thorax 1979;34:166–76.
9. Lentz DJ, Pollock EM, Olsen DB, Andrews EJ, Murashita J, Hastings WL. Inhibition of mineralization of glutaraldehyde-fixed Hancock bioprosthetic heart valves. In: Cohn LH, Gallucci V, eds. Cardiac bioprostheses. New York: Yorke Medical, 1982:306.
10. Carpentier A, Nashef A, Carpentier S, Ahmed A, Goussef N. Techniques for prevention of calcification of valvular bioprostheses. Circulation 1984;70(Suppl 1):165–8.
11. Magilligan DJ Jr, Lewis JW Jr, Stein P, Alam M. The porcine bioprosthetic heart valve: experience at 15 years. Ann Thorac Surg 1989;48:324–30.
12. Perier P, Deloche A, Chauvaud S, et al. A 10-year comparison of mitral valve replacement with Carpentier-Edwards and Hancock porcine bioprostheses. Ann Thorac Surg 1989;48:54–9.
13. Hartz RS, Fisher EB, Finkelmeier B, et al. An eight-year experience with porcine bioprosthetic cardiac valves. J Thorac Cardiovasc 1986;91:910–7.
14. Jamieson WRE, Allen P, Miyagishima RT, et al. The Carpentier-Edwards standard porcine bioprosthesis. A first-generation tissue valve with excellent long-term clinical performance. J Thorac Cardiovasc Surg 1990;99:543–61.
15. Jamieson WRE, Tyers GF, Miyagishima RT, Germann E, Janusz MT, Ling H. Carpentier-Edwards porcine bioprostheses. Comparison of standard and supra-annular prostheses at 7 years. Circulation 1991;84(Suppl 3):145–52.
16. Akins CW, Carroll DL, Buckley MJ, Daggett WM, Hilgenberg AD, Austen WG. Late results with Carpentier-Edwards porcine bioprosthesis. Circulation 1990;82(Suppl 4):65–74.
17. Bernal JM, Rabasa JM, Cagigas JC, Echevarria JR, Carrion MF, Revuelta JM. Valve-related complications with the Hancock I porcine bioprosthesis. A twelve- to fourteen-year follow-up study. J Thorac Cardiovasc Surg 1991;101:871–80.
18. David TE, Ho WIC, Christakis GT. Thromboembolism in patients with aortic porcine bioprostheses. Ann Thorac Surg 1985;40:229–33.
19. Levine FH, Carter JE, Buckley MJ, et al. Hemodynamic evaluation of Hancock and Carpentier-Edwards bioprostheses. Circulation 1981;64(Suppl 2):192–5.
20. Khan S, Mitchell RS, Derby GC, Oyer PE, Miller DC. Hemodynamic comparison of Hancock and Carpentier-Edwards mitral bioprosthetic valves. Circulation 1990;82(Suppl 4):75–81.

DISCUSSION

DR JAVIER FERNANDEZ (Browns Mills, NJ): Dr David, I know that you do a lot of valve repairs. How do you compare your results of valve repair with the results of these Hancock valves in terms of valve-related complications and reoperation?

DR DAVID: I have repaired aortic valves only in the past 3 or 4 years, so I cannot make any comments on the long-term complications. I have been repairing mitral valves for more than a decade, and valve-related complications are uncommon. I do not know if it is reasonable to compare patients who had mitral valve repair with those who had mitral valve replacement because the pathologic process in the mitral valve is often different. I am able to repair the mitral valve in most patients with myxomatous disease, less than half of the patients with rheumatic disease, and only a few with ischemic mitral insufficiency. I should tell you that we have an ongoing cohort study of patients who had mitral valve repair or replacement with and without preservation of chordae tendineae. I do not know details of valve-related complications, but the actuarial survival after mitral valve replacement with preservation of chordae tendineae is much better than after mitral valve replacement with excision of the mitral apparatus, and it is not much different than that of mitral valve repair. We will present these data in the near future.

DR W. R. E. JAMIESON (Vancouver, BC, Canada): Dr David, we congratulate you on the very excellent evaluation of the Hancock II porcine bioprosthesis. As Dr Miller has stated, we have been anticipating your evaluation of this new prosthesis for some time. We, at the University of British Columbia, have experience with the Carpentier-Edwards Supra-Annular porcine bioprosthesis, which is the other second-generation prosthesis that has low-pressure glutaraldehyde tissue fixation. We have documented our experience at 8 years indicating very comparable results. These two new porcine bioprostheses have provided satisfactory clinical performance. I have one question for your consideration, related to the freedom from stroke of 90%. Is this freedom from permanent neurological deficit, and have you considered the composite evaluation of valve-related mortality and residual morbidity related to valve-related neurological events, which provides an indication of the quality of life of patients with bioprostheses?

DR DAVID: I used your article on the performance of the Carpentier-Edwards bioprostheses for comparison with our results. You were the first to describe this parameter of valve-related complication, namely, the valve-related mortality and residual morbidity. We did not look into the residual morbidity in our analysis. We defined a transient ischemic attack as a neurologic deficit that resolved completely within 30 minutes, and stroke as a neurologic deficit that lasted longer than 30 minutes and may have been permanent. There was a high mortality among these patients; in the aortic valve replacement group there were 8 strokes with one death, and in the mitral valve replacement group there were 14 strokes with six deaths. That was one of the reasons why I presented transient ischemic attacks and strokes separately.

DR JOHN E. HUTCHINSON III (Hackensack, NJ): I am concerned because I do so many reoperations on people who have biological prostheses. The number of reoperations keeps going up and up and up. I have always tried, in my practice, to pick a valve that suits the patient, and I have always believed that in patients who are going to be on chronic anticoagulation therapy, there is no specific advantage in using a bioprosthesis with the greater probability of reoperation. In your patient population, do you consider the need for chronic anticoagulation therapy as a relative contraindication for use of a tissue valve?

DR DAVID: I agree with you that if a patient is in chronic atrial fibrillation and is going to require life-long anticoagulation with warfarin, it may be inappropriate to use a bioprosthesis. As far as the type of valve a patient should have, I believe that the patient, his or her family, the family doctor, and the cardiologist should participate in the decision-making. I have always tried to match the patient to the heart valve prosthesis as far as types and sizes are concerned.

Like you, I frequently operate on patients with failed bioprostheses, and often I implant another bioprosthesis because the patient wishes to have this type of valve. I guess warfarin interferes too much with their life-style.

Use of Epicardial Electrocardiograms for Detecting Cardiac Allograft Rejection

Eric D. Irwin, MD, Richard W. Bianco, BS, Rose Clack, BS, John Grehan, BA,
David P. Slovut, MD, Raouf Nakhleh, MD, R. Morton Bolman III, MD, and
Sara J. Shumway, MD

Division of Cardiovascular and Thoracic Surgery and Department of Laboratory Medicine and Pathology, University of Minnesota Hospitals, Minneapolis, Minnesota

Since the advent of cyclosporin A surface electrocardiograms have been unreliable for diagnosing cardiac allograft rejection. Although several noninvasive methods have been proposed, none have been sufficiently accurate to be considered for clinical use. We have studied the use of the QRS complex amplitude, the unipolar peak-to-peak amplitude, recorded from intramyocardial electrodes for detecting rejection. Ten adult mongrel dogs underwent placement of intramyocardial electrodes on each ventricle. After stabilization of signals the hearts were transplanted heterotopically into unmatched recipients receiving cyclosporin A, azathioprine and methylprednisolone. Endomyocardial biopsies were performed after stabilization of unipolar peak-to-peak amplitude, twice weekly thereafter, and when unipolar peak-to-peak amplitude fell significantly. This detected 13 of 14 episodes of rejection. There was one false-positive and one false-negative result. The false-negative study became positive the following day. Thus, analysis of unipolar peak-to-peak amplitude detected all episodes of rejection in a clinically relevant time frame and was able to detect mild forms of rejection and multiple episodes of rejection in the same heart even in the presence of therapeutic levels of cyclosporin A.

(Ann Thorac Surg 1992;54:669–75)

The diagnosis of rejection in patients who have undergone cardiac transplantation continues to be a problem without an ideal solution. To date rejection can be diagnosed only by the use of serial percutaneous transvenous endomyocardial biopsies (EMBs). There are, however, a number of problems with the use of EMBs for the diagnosis of rejection.

First, inadequate tissue is obtained for proper assessment in up to 6% of biopsies [1], and even with apparently adequate tissue EMBs are reported to have a 15% false-negative rate [2]. Second, obtaining a biopsy specimen is an invasive procedure that is associated with a small but not insignificant risk of complication [3–5]. Third, biopsies are expensive and can be performed only in specialized centers. Fourth, the time required for tissue processing results in an 8- to 24-hour delay in obtaining the diagnosis. Finally, biopsies cannot be performed frequently enough to assure that rejection will be diagnosed in its earliest stages when damage to the transplanted heart is only minimal. Thus a widely available, noninvasive method for detecting the onset and reversal of cardiac allograft rejection is needed. This will allow patients to be followed up more closely, and at a lower risk to the patient as well as at a lower cost.

Several noninvasive techniques have been used in the past for detecting allograft rejection. They have, however, generally reported results that lacked sufficient accuracy for determining clinical therapy in cardiac transplant recipients. During the initial decade of cardiac transplantation the results of several studies suggested that changes in the amplitude of the QRS complex measured from standard 12-lead electrocardiograms could be used to detect severe rejection [6, 7]. With the advent of cyclosporin A (CSA) this is no longer true [8, 9].

Analysis of R-wave voltage, the peak-to-peak amplitude of unipolar electrograms (UPPA), obtained from intramyocardial plunge electrodes has been shown to be an accurate, sensitive, and quantitative predictor of local irreversible myocardial ischemic injury [10]. In this study the UPPA decrease correlated closely with the local histological changes that subsequently developed. With initially encouraging results in ischemic preparations other investigators applied this method to the diagnosis of rejection in patients after cardiac transplantation. Wahlers and colleagues [11] studied 13 patients who underwent orthotopic cardiac transplantation with simultaneous implantation of a telemetric pacemaker. Voltages were measured from electrodes placed on the right atrium and ventricle. They found that signals recorded via standard telemetry units failed to provide adequate accuracy for determining therapy in patients.

Rosenbloom and colleagues [12] circumvented some of these problems by recording intramyocardial electrograms directly from epicardial pacing electrodes. Electrodes were placed on the anterior and posterior aspect of

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Shumway, Division of Cardiovascular and Thoracic Surgery, University of Minnesota, UHMC Box 207, Minneapolis, MN 55455.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

each ventricle. By avoiding the use of telemetry they were able to demonstrate significantly better results, with a 100% sensitivity and a 91% specificity. Thus UPPA recorded directly from four ventricular epicardial pacing electrodes detected rejection in cardiac allografts with sufficient accuracy to be considered for clinical application. There were, however, three questions that remained unanswered by this study: (1) would the use of CSA adversely affect the accuracy of this method as it had with standard 12-lead electrocardiograms, (2) could this method be used for detecting repetitive episodes of rejection in the same heart, and (3) could mild forms of rejection be detected using this technique? The following study was designed to answer these questions as well as to further test the use of UPPA for diagnosing rejection.

Material and Methods

All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" as published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

Abdominal Heterotopic Transplantation

Our first four studies used heterotopic transplantation in the abdomen. The heart from an unmatched donor dog was procured after preservation with potassium crystalloid cardioplegia and topical hypothermia with iced saline solution. After explantation of the heart the superior vena cava, inferior vena cava, and pulmonary veins were ligated. The donor aorta and pulmonary artery were then prepared.

The recipient animal was anesthetized with sodium pentothal and placed on a ventilator for maintenance anesthesia with halothane and oxygen. A laparotomy was then performed, and the infrarenal inferior vena cava and aorta were isolated. Anastomoses of the donor pulmonary artery to the recipient inferior vena cava and the donor aorta to recipient aorta were fashioned using continuous monofilament suture. The heart was then deaired by removal of the pulmonary artery clamp and venting of the aorta. After this, arterial blood flow was restored and the heart defibrillated. A biopsy cannula was then placed through the free wall of the right ventricle, and screw-in epicardial pacing electrodes (Medtronic, Inc, Minneapolis, MN) were affixed to the anterior and posterior aspect of each ventricle. The electrodes were then connected to a block that allowed direct percutaneous electrical connections to be made. The electrode block and biopsy cannula were then placed in subcutaneous pockets, and the abdomen was closed in layers.

Thoracic Heterotopic Transplantation

Eight adult mongrel dogs received thoracic heterotopic cardiac transplants as previously described [13]. The heart from an unmatched donor was procured as described for abdominal transplantation. After explantation of the heart an atrial septal defect was created and the mitral valve rendered incompetent. This provided optimal decompression of the left ventricle. The pulmonary valve was also rendered incompetent. This reduces the tendency for the right ventricular volume to decrease with time, as is seen in the unloaded heart, and facilitates performance of EMB. The superior and inferior venae cavae were then ligated and the pulmonary veins oversewn. The donor aorta and pulmonary artery were then prepared for anastomosis.

The recipient animal was anesthetized with sodium pentothal, placed on a ventilator, and maintained under general anesthesia using halothane and oxygen. Through a left thoracotomy, the recipient superior vena cava and left innominate artery were mobilized. End-to-side anastomosis of the donor pulmonary artery to the recipient superior vena cava was performed with continuous monofilament suture. Similarly, the donor aorta was anastomosed to the recipient left innominate artery. Upon completion of the anastomoses venous clamps were removed and the heart deaired. After this, arterial blood flow was restored and the heart defibrillated. A biopsy cannula was then affixed to the free wall of the right ventricle. This model provides a heart that is perfused and contracting in a nonworking setting with electrical activity.

The chest incision of the recipient was then closed in layers, and the biopsy cannula and electrode block were placed in separate subcutaneous pockets. The animal was then allowed to awaken and was taken to the postoperative care facility.

Electrodes

Sutureless intramyocardial screw-in electrodes (Medtronic, Inc) were placed on the anterior and posterior aspects of each ventricle of the donor animal. These were brought through the chest wall to a subcutaneous pocket, where they were affixed to a block that allowed direct electrical connection to be made with the epicardial pacing electrodes. The posterior surface of the block contained a standard indifferent electrode.

Immunosuppression Protocol

Each recipient animal received CSA (18 $mg \cdot kg^{-1} \cdot day^{-1}$) and azathioprine (3 $mg \cdot kg^{-1} \cdot day^{-1}$) starting 2 days before transplantation and continuing postoperatively. On the day of transplantation methylprednisolone (1 g as an intravenous bolus) was given preoperatively. This dose was continued through postoperative day 3. On postoperative day 4 this was decreased to 500 mg intravenously and then 125 mg intravenously on postoperative day 5. After this, the animals received methylprednisolone (1 $mg \cdot kg^{-1} \cdot day^{-1}$). After stabilization of voltages recorded from the endomyocardial electrodes, an EMB was performed. After tissue verification of viable nonrejecting myocardium the methylprednisolone was tapered. If after 3 days there was no evidence of rejection, administration of azathioprine and methylprednisolone was discontinued and CSA administration was maintained at therapeutic levels. If after 5 additional days there was no evidence of rejection CSA doses were reduced by one half. After 3 to 5 days if there was no evidence of rejection the administration of CSA was discontinued until biopsy confirmation of rejection was obtained. After biopsy confirmation of rejection immunosuppression identical to that used in the immediate postoperative period was resumed.

Unipolar Peak-to-Peak Amplitude Data Acquisition

Starting on postoperative day 1 intramyocardial electrograms were recorded daily. The initial data acquisition system consisted of a variable-gain signal amplifier with filter settings of 1,000 Hz high-pass and 0.05 Hz low-pass. Data were then recorded using an analog-to-digital converter (Dataque Instruments, Akron, OH) installed in a personal computer. At present we use a four-channel electrocardiogram isolation unit and amplifier, with the same filter settings, coupled to the analog-to-digital converter for data acquisition.

Unipolar Peak-to-Peak Amplitude Analysis

Data for each lead were obtained by averaging the QRS amplitudes of 10 beats. Daily average voltage for each electrode was compared with the maximum average voltage obtained in the three previous determinations (reference voltage). The averaged voltage for a given day was divided by the reference voltage for that electrode and expressed as a percent. This process was repeated with each average daily voltage compared with the previous days' average daily voltage. The ratios for the four leads were averaged to determine the total percent retained UPPA. A total UPPA decline of greater than 15% for the four-lead average, compared with the reference value for the previous 3 days, or a decline of greater than 9% over 1 day was considered indicative of rejection necessitating EMB for tissue confirmation.

Endomyocardial Biopsy

Endomyocardial biopsy specimens were obtained after stabilization of recorded voltages, usually occurring between postoperative days 5 and 8, twice weekly thereafter, and when criteria for UPPA reduction were present. Biopsies were performed using standard cardiac biopsy forceps (Cordis) or rigid bronchoscopy biopsy forceps. To perform an EMB animals were lightly anesthetized with sodium pentothal and the subcutaneous pocket containing the biopsy cannula was opened using sterile technique. The forceps were then advanced through the cannula and multiple specimens obtained. At the completion of the study the animals were sacrificed. The transplanted hearts were then explanted for gross and microscopic examination.

Histologic Grading

All biopsy specimens were evaluated by a cardiac pathologist who was unaware of the UPPA findings or physiological state of the heart. Cardiac samples were graded histologically according to the criteria of Billingham and colleagues [14]. All specimens obtained at postmortem examination were examined and graded in a similar manner.

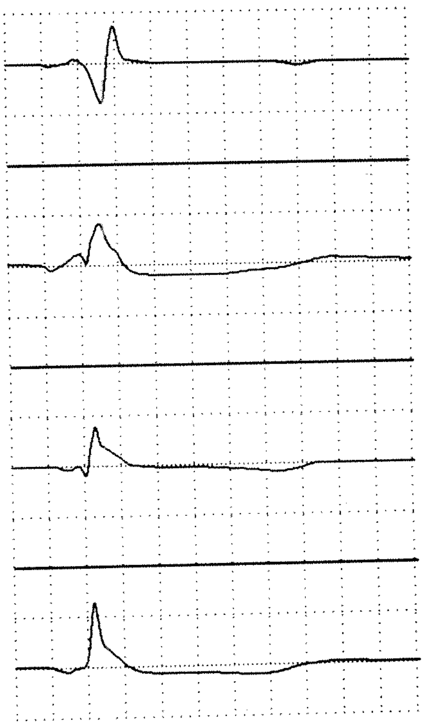


Fig 1. Example of electrocardiograms recorded from intramyocardial electrodes: a representative four-lead electrocardiogram recorded using the electrocardiogram isolation unit with low-pass and high-pass filter settings of 0.05 Hz and 1,000 Hz, respectively.

Results

An example of a daily tracing recorded from the four epicardial leads is shown in Figure 1. We have found a large number of biphasic QRS complexes in our data; as a result, we use the difference in voltage between the most negative and the most positive deflections of the QRS complex to determine the amplitude of the QRS complex for UPPA calculations. Unipolar peak-to-peak amplitude calculations were carried out as described in the Material and Methods section. Figure 2 shows the time course of UPPA changes, expressed as a percentage of the reference value from the previous 3 days. This is plotted against days after transplantation. This figure demonstrates changes in UPPA that detected three biopsy-proven episodes of rejection in the same animal. These occurred in the presence of therapeutic CSA levels throughout the course of the study.

Thirteen of 14 biopsy-confirmed episodes of rejection were detected using a 15% reduction in UPPA compared with the greatest reference voltage of the previous 3 days or a 9% decrease from the previous day. No evidence of rejection was seen in eight of nine biopsy specimens obtained when UPPA criteria for rejection were absent. There was one episode of rejection that was not detected by strict UPPA criteria; this represented the only false-negative result in our study. There was one false-positive UPPA study in our experiment. This represents a sensitivity of 93% and a specificity of 88% for the diagnosis of rejection in this canine model of cardiac allograft trans-

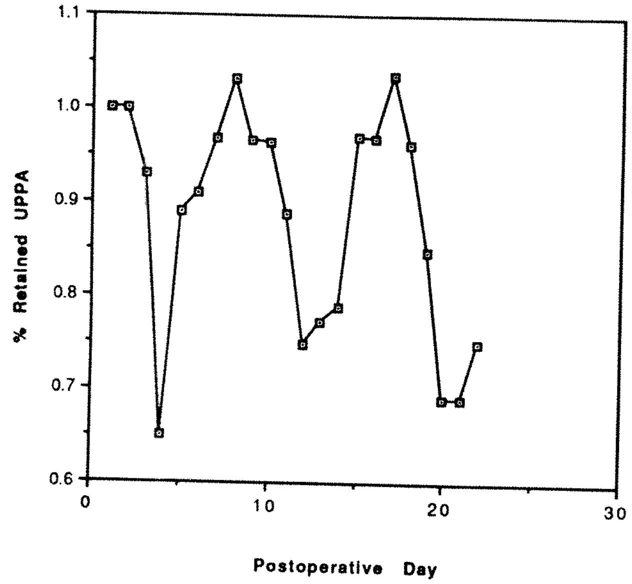


Fig 2. Changes in percent retained unipolar peak-to-peak amplitude (UPPA) that detected three episodes of biopsy-proven rejection in the same transplant recipient.

plantation. It should be noted, however, that the UPPA for the one false-negative study became positive the following day and a repeat biopsy demonstrated rejection. Thus UPPA detected all episodes of rejection in a clinically relevant time frame. The sensitivity for detecting episodes of rejection in a clinically relevant time frame was 100%. We believe that including this data point is justified because clinically EMBs are performed at intervals of 1 to 2 weeks or more.

Additionally, in this study there were four episodes of mild rejection and three episodes of moderate rejection. All of these rejection episodes were correctly diagnosed by analysis of UPPA recorded from intramyocardial electrodes.

To help explain the difference between this analysis and that of other authors we analyzed our data using alternative lead combinations. We reanalyzed the electrocardiographic data from the last six transplants and calculated UPPA for two- and three-lead combinations. Table 1 shows the sensitivity of two- and three-lead combinations for diagnosing rejection for the last six transplants. As can be seen, no lead combination with less than four leads approached the diagnostic accuracy obtained by using all four leads for analysis.

Table 1. Sensitivity of Lead Configurations Using Fewer Than Four Electrodes

Electrode Configuration	Sensitivity
LVA + LVP	47%
RVA + RVP	35%
LVA + RVA	41%
LVP + RVP	47%
LVA + LVP + RVA	53%
LVA + LVP + RVP	53%
LVA + LVP + RVA + RVP	100%[a]

[a] In a clinically relevant time frame; see text for discussion.

LVA = anterior aspect of the left ventricle; LVP = posterior aspect of the left ventricle; RVA = anterior aspect of the right ventricle; RVP = posterior aspect of the right ventricle.

Twelve of the 14 episodes of rejection in this study occurred while therapeutic doses (9 mg/kg twice per day) were being administered. In 7 of these cases therapeutic levels of CSA (>150 μg/L) were present. Cyclosporin A levels were subtherapeutic in the remaining 7 cases, less than 100 μg/L in 4 and 100 to 149 μg/L in the remaining 3 episodes of rejection.

Comment

These data demonstrate that the analysis of UPPA measured from intramyocardial electrograms is capable of detecting rejection with sufficient accuracy to be considered for clinical application. This method remains valid even in the presence of therapeutic levels of CSA and can be used to detect repeated episodes of rejection within the same heart. This is important as it may reduce the number of endomyocardial biopsies needed for diagnosing rejection.

The use of percutaneous transvenous EMB was originally described by Sakakibara and Konno in 1962 [15] and subsequently adapted for monitoring rejection in cardiac transplant recipients by Caves and colleagues in 1973 [16]. This method, however, suffers from several limitations. First, obtaining a biopsy specimen is an invasive procedure that is associated with a small but not insignificant risk of complication. This is demonstrated in one recent series, at a major transplant center, where the incidence of complications associated with EMB was reported to be between 0.3% and 1.3% [3]. These complications included local infection, pneumothorax, and rupture of the right ventricle with hemorrhage [3]. Furthermore, with EMB inadequate tissue is obtained in up to 6% of biopsies [1]. Even with apparently adequate tissue, EMB is reported to have a 15% false-negative rate [2]. This is believed to occur because of the more patchy infiltrates seen in the rejecting myocardium of patients treated with CSA-based immunotherapy. Thus the use of EMB fails to provide the ideal level of accuracy. A second problem with the use of biopsies is the expense. This is particularly important as EMBs are currently used primarily for screening purposes. Thus a noninvasive, less expensive, method is needed to reduce the number of biopsy specimens obtained for surveillance purposes alone. This will allow closer follow-up for the patients at a lower risk and with lower health care costs. A third problem with EMBs is that they can be performed only in specialized centers. This results in substantial expense for the patient and can cause a delay in the diagnosis if patients must be transferred to special centers. Additional delays in diagnosis result from the time required for tissue processing once the biopsy specimen is obtained. This results in an additional delay of 8 to 24 hours before pathology results are available and the diagnosis of rejection is confirmed or excluded. The analysis of UPPA is straightforward and can be performed with minimal delay. A final problem with EMB is seen in the late posttransplant period when biopsies cannot be performed frequently enough to ensure that rejection will be diagnosed in its earliest stages. Thus a widely available, noninvasive method for detecting the onset and reversal of cardiac allograft rejection is needed. Even though the need for EMB may not be eliminated by such a method, a reduction in the number of biopsies is desirable. Our results suggest that analysis of UPPA from four epicardial electrodes can fill this need as it allows closer follow-up for patients at a lower risk with lower health care costs.

The exact cellular processes responsible for the electrocardiographic changes seen during allograft rejection are not clearly understood. Cellular changes seen during acute allograft rejection in patients treated with azathioprine and methylprednisolone consist of diffuse edema, leukocyte infiltration, and myocardial necrosis. These changes are thought to be responsible for alterations in the cardiac action potential, which result in the voltage decline seen in standard electrocardiograms during episodes of acute rejection. With the addition of cyclosporine to immunosuppressive regimens rejection is changed to a process characterized by patchy areas of focal rejection with minimal edema. This has resulted in the loss of consistent changes in surface electrocardiograms associated with the rejection process. Thus standard surface electrocardiograms are no longer sufficiently accurate to be considered clinically applicable [8, 9].

Other conditions are known to reduce the accuracy of standard 12-lead electrocardiograms and the more sophisticated forms of analysis of electrocardiograms recorded from electrodes placed on the skin surface. These include the presence of pericardial or pleural effusions, edema, sepsis, pneumothorax, or pulmonary consolidation. In their series Keren and associates [17] found that postoperative changes in the mediastinum prevented signal-averaged electrocardiograms from diagnosing rejection in the early posttransplantation period. Analysis of UPPA from intramyocardial electrodes offers the advantage of assessing the heart independent of these changes and provides important advantages for diagnosing rejection in cardiac transplant recipients. During the early posttransplantation period Keren and colleagues [17] also found that signal averaging of surface electrocardiograms could not reliably diagnose mild forms of rejection. In this study we were able to detect even mild forms of rejection.

In the current study we found that electrograms recorded from intramyocardial electrodes were more accurate in diagnosing rejection than other authors have reported [11, 18]. We believe that this can be accounted for by differences in instrumentation. Wahlers and associates [11] have evaluated the use of electrodes placed on the epicardial surfaces of the right atrium and right ventricle in patients undergoing orthotopic cardiac transplantation. Monitoring voltages from these electrodes via a telemetric pacemaker they were unable to correlate histologic grades of rejection with corresponding changes in voltages recorded from the electrodes. Warnecke and associates, using similar instrumentation, reported an 87.9% sensitivity for detecting rejection in human allografts. We believe that our ability to detect all episodes of rejection is the result of using four electrodes. As the rejection process is occasionally patchy, four electrodes may detect an episode that would have been missed by a single electrode. This is shown in Table 1, where combinations of two or three leads demonstrated sensitivities of 53% or less.

Avitall and colleagues [18] examined the electrophysiologic changes occurring during acute rejection of heterotopic cardiac allografts using a canine model in which no immunosuppression was given. They also failed to find correlations between changes in the UPPA and either mild or moderate rejection. There are, however, several differences between the current study and the work of Avitall and colleagues. First, when immunosuppression is not used, stabilization of the tissue-electrode interface does not occur. Without such a period of stabilization it is very difficult to differentiate the effects of rejection from the short-term tissue-electrode interactions. Our work as well as that of others [12, 14] has shown that a period of 5 days is needed to allow stabilization. In our current protocol we implant the electrodes at least 7 to 10 days before transplantation to allow stabilization. In the clinical setting, where the donor and recipient have the same blood type, rejection during the first 7 days is unusual and thus an adequate time period for stabilization is present. Furthermore, a biopsy specimen obtained 7 to 10 days after transplantation would be very desirable, so as to provide a baseline for further comparison. Thus a period of nearly 2 weeks would be available for stabilization of tissue-electrode interactions. This period could be modified further if long-term studies demonstrated this to be necessary. Finally, the present study, as did the work of Rosenbloom and colleagues [12] compares daily UPPA values with data recorded over the preceding 3 days. This tends to neutralize the more long-term effects of electrode-tissue interactions seen over weeks or months. Studies of longer duration are needed to determine the optimal interval for data acquisition in the chronic setting.

An additional use of this technology could be the early detection of allograft atherosclerosis. As previously reported [10], ischemia may produce abrupt and substantial declines in the UPPA. Exercise-induced regional ischemia could readily be identified by the local intramyocardial electrode in the ischemic region.

Finally, with the application of this technology, one should be able to increase the intervals between biopsies. If the average UPPA remains unchanged, biopsy would be safely postponed until it was indicated clinically. If a decrease in UPPA was noted and rejection clinically suspected, a biopsy would be performed for verification. As UPPA decline occurs early in the time course of acute allograft rejection, this information may lead to earlier detection of episodes of rejection. This would allow treatment to be instituted more expeditiously and limit damage to the graft.

In conclusion, UPPA analysis using four intramyocardial screw-in electrodes provides a noninvasive, highly sensitive, and specific indicator of cardiac allograft rejection. Its application may substantially reduce the number of EMBs needed and allow for closer follow-up at less risk to the patient and at lower cost to the health care system.

We acknowledge financial support provided by Medtronic Inc, who provided partial funding for this work by a Synergy Technology Transfer Award (Medtronic Inc, Minneapolis, MN).

References

1. Cooper DKC, Fraser RC, Rose AG, et al. Technique, complications and clinical value of endomyocardial biopsy in patients with heterotopic heart transplants. Thorax 1982;37: 727–31.
2. Sibley RK, Olivari MT, Ring WS, Bolman RM. Endomyocardial biopsy in cardiac allograft recipient: a review of 570 biopsies. Ann Surg 1986;203:177–87.
3. Anastasiou-Nana MI, O'Connell JB, Nanas JN, et al. Relative efficiency and risk of endomyocardial biopsy: comparison in heart transplant and nontransplant patients. Cathet Cardiovas Diagn 1988;18:7–11.
4. Parrillo JE, Aretz HT, Palacios I, et al. The results of transvenous endomyocardial biopsy can frequently be used to diagnose myocardial diseases in patients with idiopathic heart failure. Endomyocardial biopsies in 100 consecutive patients revealed a substantial incidence of myocarditis. Circulation 1984;69:93–101.
5. Nippoldt TB, Edwards WD, Holmes DR, et al. Right ventricular endomyocardial biopsy. Clinicopathologic correlates in 100 consecutive patients. Mayo Clin Proc 1982;57:407–18.
6. Hess ML, Hastillo A, Wolfgang TC, et al. The noninvasive diagnosis of acute and chronic cardiac allograft rejection. J Heart Transplant 1981;1:31–8.
7. Oyer PE, Stinson EB, Bieber CT, et al. Diagnosis and treatment of acute cardiac allograft rejection. Transplant Proc 1979;11:296–303.
8. Haberl R, Weber M, Reichenspurner H, et al. Frequency analysis of the surface electrocardiogram for recognition of acute rejection after orthotopic cardiac transplantation in man. Circulation 1987;76:101–8.
9. Cooper DKC, Charles RG, Rose AG, et al. Does the electrocardiogram detect early acute heart rejection? J Heart Transplant 1985;4:546–8.
10. Lofland GK, German LD, Ross M, et al. The local unipolar depolarization complex: a quantitative electrophysiologic index of irreversible myocardial ischemic injury. Surg Forum 1984;35:269–71.
11. Wahlers T, Haverich A, Schafers HJ, et al. Changes of the intramyocardial electrogram after orthotopic heart transplantation. J Heart Transplant 1986;5:450–4.
12. Rosenbloom M, Laschinger JC, Saffitz JE, et al. Noninvasive detection of cardiac allograft rejection by analysis of the unipolar peak-to-peak amplitude of intramyocardial electrograms. Ann Thorac Surg 1989;47:407–11.
13. Jamieson SW, Burton NA, Reitz BA, et al. A new method for heterotopic cardiac transplantation in the dog. J Surg Res 1982;32:150–3.
14. Billingham ME, Cary NRB, Hammond ME, et al. A working formulation for the standardization of nomenclature in the diagnosis of heart and lung rejection: Heart Rejection Study Group. J Heart Transplant 1990;9:587–93.
15. Sakakibara S, Konno S. Endomyocardial biopsy. Jpn Heart J 1962;3:537–43.
16. Caves PK, Stinson EB, Graham AF, et al. Percutaneous transvenous endomyocardial biopsy. JAMA 1973;225:288–91.
17. Keren A, Gillis AMM, Freedman RA, et al. Heart transplant rejection monitored by signal-averaged electrocardiography in patients receiving cyclosporin. Circulation 1984;70(Suppl 1):124–9.
18. Avitall B, Payne DD, Connolly RJ, et al. Heterotopic heart transplantation: electrophysiologic changes during acute rejection. J Heart Transplant 1988;7:176–82.

DISCUSSION

DR T. BRUCE FERGUSON (St. Louis, MO): I would like to endorse the concept of this type of monitoring of cardiac transplantation, but I have several questions for the group from Minneapolis. We have recently completed a number of studies looking at this same type of technology, some of which were published in *Circulation* several months ago and additional data that were presented at the meeting of the Western Thoracic Surgical Association last year. The difference between our studies and your study have to do with the analysis and recording of the intramyocardial electrograms.

We have found that if the data are obtained in a way that allows pure recording of the UPPA, the mathematical summation of the different epicardial electrograms is really not necessary. We demonstrated in our article published in *Circulation* that there are two-, three-, and four-electrode combinations that can be used, but if the algorithms used to determine the amplitude of the peak to peak potential are done in a way we would consider to be proper, you can get the same information recording absolute amplitude values from as few as two electrograms. These results have been confirmed by the group at the Berlin Heart Center as well, both experimentally and clinically.

So my first question is, do you have an explanation for this discrepancy and for the low sensitivity and specificity associated with your individual amplitude recordings from the individual electrodes? Second, are you attempting to address this problem in any future studies, as obviously this is a technique that is applicable to pacemaker telemetry technology, which cannot be done if you need four electrograms to be able to perform the analysis? And finally, have you attempted any of these types of studies in your transplant patient population at the University of Minnesota?

DR IRWIN: Thank you very much for your comments. We have also looked at alternative ways of calculating UPPA. Specifically, we have summed the voltage of the four leads and compared this with the summed voltages of the 3 previous days. Using this we have found that there is no change in accuracy for detecting rejection, a finding similar to what you have discussed.

As to the optimal number of leads, our data suggest that the use of four leads adds significantly to the sensitivity of the method, particularly for detecting milder forms of rejection. In the literature many of the episodes of rejection that were detected using fewer leads were more advanced than those that we were able to detect using four leads. I am unaware of any other factors that could account for this disparity.

DR AXEL HAVERICH (Hannover, Germany): At our institution we have been very interested in this electrocardiogram for noninvasively detecting cardiac allograft rejection, and we started implanting telemetric pacemaker systems in these patients in 1983. After a study period of about 2 years, we were so disappointed clinically that we stopped using this methodology for detecting allograft rejection.

Now, after more than 5 years of follow-up, we took 20 long-term survivors after cardiac transplantation and revitalized this study. Looking at telemetric electrocardiographic amplitudes, both for the atrial and the ventricular part, we saw a tremendous shift in the R waves in these patients over the years. In some, the R waves had increased by more than 200%; in some they were down by 100 to 120%. Therefore, I think one of the major issues of noninvasive cardiac allograft surveillance, namely, the late detection, will be impossible by using this system.

DR IRWIN: In this study we have no data evaluating changes in baseline voltages occurring over periods of 3 to 5 years. In our protocol we compare the daily voltage with the peak voltage of the 3 previous days to account for variation in the baseline. Clearly, the optimal interval between electrocardiograms that will allow one to account for variation in baseline, without reducing the sensitivity of the method, needs to be addressed in clinical studies.

DR PETER W. BARRETT (New Haven, CT): I have two quick questions. First, somehow I do not quite consider this noninvasive in that everybody does not like to leave hardware in a transplant patient. Do you know or are you worried about an increased incidence of infection? Second, you mentioned that it is detecting earlier rejection, but we all often do not treat earlier rejection. Have you had any work with biopsy results that correlate with myocyte necrosis?

DR IRWIN: In this study we were able to detect a wide range of severities of rejection, including some early grades that would not necessarily be treated. In our data approximately one half of the episodes were associated with more severe myocyte necrosis. These cases correlated with more profound changes in voltages. The magnitude of change in voltage that would be treated would need to be addressed in more detail in clinical trials.

As to the issue of leaving hardware in the patient, we are also concerned about the associated risk of infection. We are anxiously awaiting the development of telemetric pacemakers that have sufficient accuracy to resolve, within a few percent, differences in voltages. Then this technology can be applied clinically using telemetry rather than requiring percutaneous access.

Notice From The Society of Thoracic Surgeons

The Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons will be held at the San Antonio Convention Facility in San Antonio, Texas, January 25–27, 1993. There is no registration fee for the meeting for members of The Society. The registration fee is also waived for speakers, residents, and fellows. A $250.00 guest registration fee will apply to all other nonmember physicians.

The Twenty-sixth Postgraduate Course is scheduled for Sunday, January 24, 1993. The registration fee is $65.00 for all attendees. The Postgraduate Program will include minisymposia dealing with Thoracoscopy, Current Pulmonary Surgical Problems, Decisions in Cardiac Surgery, and Transplantation. A C.C.C.E.T.S. Basic Science Lecture and a special luncheon presentation by Floyd Loop on a subject of general interest will also be included.

In addition to the Postgraduate Program, this year's Annual Meeting will include a scientific poster session, breakfast seminars, the annual movie night, a wide range of surgical exhibits, and a complete schedule of scientific presentations drawn from the largest volume of abstracts ever submitted for presentation to The Society.

An advance program information booklet will be mailed to all members of The Society this fall. It will include a detailed schedule of events as well as registration and housing forms and other pertinent information regarding the Annual Meeting. Nonmembers wishing to receive the advance program booklet should write to the Secretary of The Society, Richard P. Anderson, MD.

Richard P. Anderson, MD
Secretary
The Society of Thoracic Surgeons
401 N Michigan Avenue
Chicago, IL 60611
(312) 644-6610
FAX (312) 527-6635

Predictive Criteria for the Need of Extracorporeal Circulation in Single-Lung Transplantation

Stephan W. Hirt, MD, Axel Haverich, MD, Thorsten Wahlers, MD,
Hans-Joachim Schäfers, MD, Aiman Alken, MD, and Hans-Georg Borst, MD

Division of Thoracic and Cardiovascular Surgery, Surgical Center, and Department of Anesthesiology, Hannover Medical School, Hannover, Germany

Use of extracorporeal circulation is mandatory in heart-lung and en bloc double-lung transplantation. However, no criteria exist to predict the necessity of its application during single-lung transplantation for parenchymal lung diseases. We therefore reviewed our experience in 23 patients undergoing single-lung transplantation for idiopathic pulmonary fibrosis. All patients were evaluated by preoperative right heart catheterization. For intraoperative monitoring, a pulmonary artery thermodilution catheter was placed in the contralateral lung to repeatedly assess pulmonary artery pressure, cardiac output, and pulmonary vascular resistance. Extracorporeal circulation was necessary during graft implantation in 4 patients, whereas 19 patients underwent operation without it. Preoperative demographic patient data, time of ischemia, and hemodynamic values obtained preoperatively and before the clamping of the pulmonary artery showed no significant differences between groups. In contrast, after the clamping of the pulmonary artery, a significant drop in cardiac index of about 1.5 L $\cdot$ min^{-1} $\cdot$ m^{-2} ($p < 0.01$) and a concomitant rise in pulmonary vascular resistance ($p < 0.01$) was observed in the group requiring extracorporeal circulation, whereas these variables showed no significant changes in the other 19 patients. Pulmonary artery pressure rose significantly in both groups ($p < 0.05$), without significant differences between them. It is concluded that intraoperative assessment of cardiac index and pulmonary vascular resistance is essential for estimation of cardiac performance during single-lung transplantation. A decrease in cardiac index of more than 1.5 L $\cdot$ min^{-1} $\cdot$ m^{-2} after the clamping of the pulmonary artery rather than the degree of pulmonary hypertension is indicative of the need of extracorporeal circulation.

(Ann Thorac Surg 1992;54:676–80)

In recent years, most of the technical problems of heart and heart-lung transplantation have been solved, leading to a high number of procedures being performed worldwide [1]. In the field of single- and double-lung transplantation, however, many questions with regard to operative strategies are still unanswered. Heart-lung and double-lung procedures using a tracheal anastomosis cannot be performed without extracorporeal circulation (ECC) [2–4]. This is also true for single-lung transplantation in patients with Eisenmenger syndrome having simultaneous repair of the cardiac defect. In contrast, ECC is not always required in patients undergoing single-lung transplantation or sequential bilateral transplantation for parenchymal lung diseases [5, 6]. However, no predictive criteria exist to determine the necessity of ECC in these patients. Preoperative hemodynamics such as right ventricular ejection fraction and pulmonary artery (PA) pressures are thought to be indicative of the need of its application, but no guidelines have been established to date. We therefore reviewed our experience in a homogeneous group of patients undergoing single-lung transplantation for idiopathic pulmonary fibrosis to establish criteria on the basis of preoperative findings and intraoperative hemodynamics.

Material and Methods

Between October 1988 and December 1991, single-lung transplantation was performed in 23 patients, 12 male and 11 female, with end-stage pulmonary fibrosis. All patients underwent right heart catheterization and respiratory function testing within 6 months before the operation. Demographic data, age, sex, body surface area, vital capacity (percent predicted), mean arterial pressure, and preoperative hemodynamics were obtained from the patients' records. Right heart catheterization included measurement of right atrial pressure, mean PA pressure (PAP), pulmonary capillary wedge pressure, and cardiac output with thermodilution technique. Cardiac index (CI) and pulmonary vascular resistance (PVR) were calculated according to standard formulas [7].

The organs were harvested from multiorgan donors in compliance with our requirements for lung donation as reported elsewhere [8]. In all donors, cold Euro-Collins solution (60 mL/kg) was used for single-flush perfusion of the PA [9–11] after previous intravenous administration of prostacyclin (prostaglandin I_2; 20 ng $\cdot$ kg^{-1} $\cdot$ min^{-1}) over a 10-minute period before aortic cross-clamping [12, 13]. After extraction of the heart, both lungs were harvested

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Hirt, Division of Thoracic and Cardiovascular Surgery, Hannover Medical School, D-3000 Hannover 61, Germany.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

en bloc and stored in an inflated state in cold Euro-Collins solution [14]. Separation of the lungs was performed immediately before implantation.

All recipients were intubated with a left-side double-lumen endotracheal tube (Robertshaw tube; Abbott-Park, Chicago, IL) and were ventilated with 100% oxygen initially. An indwelling line was inserted into the radial artery, and a thermodilution catheter was placed in the contralateral PA through the right internal jugular vein under fluoroscopic control. An oximetry catheter (Abbott-Park) was inserted through the femoral artery. Anesthesia was maintained with fentanyl (Janssen GmbH, Neuss, Germany) and midazolam hydrochloride (Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany). For relaxation, pancuronium bromide (Organon GmbH, Oberschleißheim, Germany) was used.

Mean arterial pressure, PAP, and arterial oxygen saturation were monitored continuously throughout the procedure. Thermodilution measurements of cardiac output were obtained at defined intervals: beginning with the induction of anesthesia, after placement of the patient in the lateral decubitus position, before and immediately after PA clamping, and after the declamping of the vessel.

Lung transplantation was performed through a standard thoracotomy in the fifth intercostal space. After pneumonectomy, the donor lung was implanted as described by Cooper and associates [15]. None of the patients required inotropic support before pneumonectomy. If hemodynamics deteriorated after PA clamping, catecholamines and nitrates were administered in an attempt to stabilize the circulation. In patients requiring ECC, the cannulation site was chosen based on the type of procedure performed. For right lung transplantation, cannulas were placed in the right atrium and the right femoral artery. For left lung transplantation, the PA and the left femoral artery or the descending aorta were cannulated. In all patients, a membrane oxygenator was used in the extracorporeal circuit.

After the declamping of the PA, the patients were ventilated with 50% oxygen. At the end of the operation, the double-lumen endotracheal tube was replaced by a low-pressure nasotracheal tube.

Data are expressed as the mean ± one standard deviation. Correlation analysis was performed using multiple analyses of variance of the SPSS statistical program for the IBM PC [16]. A p value of less than 0.05 was considered significant.

Results

There were no intraoperative or early postoperative deaths. In 4 patients (group 1), the hemodynamics deteriorated immediately after PA clamping and termination of ipsilateral ventilation. These patients required institution of ECC for right heart failure unresponsive to catecholamines (dopamine hydrochloride, 2 to 6 $\mu g \cdot kg^{-1} \cdot min^{-1}$; epinephrine, 0.1 to 0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$), calcium (1 g intravenously), and nitrates (nitroglycerin, 1 to 4 $\mu g \cdot kg^{-1} \cdot min^{-1}$). In 2 patients, pharmacologic stabilization was attempted repeatedly for periods of 2 to 3 minutes, and the 2 remaining patients went into progressive right heart failure after 3 and 4 minutes of this therapy. In the remaining 19 patients (group 2), the operation could be performed without bypass, but mild to moderate amounts of catecholamines and nitrates also were used.

Table 1. Recipient Preoperative Data[a,b]

Variable	Group 1 (with ECC; n = 4)	Group 2 (no ECC; n = 19)
Age at transplantation (y)	40.0 ± 8.1	47.0 ± 9.1
Male/female	2/2	10/9
BSA (m^2)	1.67 ± 0.29	1.72 ± 0.09
Preop vital capacity (% predicted)	25.3 ± 10.7	25.5 ± 5.5
Lung transplantation		
Right	2	7
Left	2	12
Ischemic time (min)	263 ± 61	249 ± 44

[a] Where applicable, data are shown as the mean ± the standard deviation. [b] There were no significant differences between groups for any of these variables.

BSA = body surface area; ECC = extracorporeal circulation.

Comparing donor data, times of ischemia, procedures performed, recipient age at transplantation, sex, and body surface area revealed no significant differences between the groups (Table 1). The donor age was 29 ± 9 years in group 1 versus 31 ± 11 years in group 2 and the partial pressure of oxygen/inspired oxygen fraction index immediately before harvesting was 442 ± 76 mm Hg in group 1 donors versus 438 ± 125 mm Hg in group 2 donors. Mean ischemic times were 263 ± 61 minutes in group 1 and 249 ± 44 minutes in group 2. In group 1, 2 right and 2 left single-lung transplantations were performed compared with 7 and 12, respectively, in group 2.

Preoperative respiratory function and right heart catheterization data also were not significantly different between the two groups. Vital capacity, mean arterial pressure, right atrial pressure, PAP, and pulmonary capillary wedge pressure were almost identical (Table 2). In group 2, the preoperative CI was lower, and therefore the calculated PVR was slightly higher than in group 1, but these differences were not significant.

Despite a significant decrease in arterial oxygen saturation in both groups after the patient was placed in the lateral decubitus position, there were no significant differences between the groups before and immediately after PA clamping (Fig 1). After declamping of the PA, arterial oxygen saturation was temporarily lower in group 1 (95.8 ± 4.7 mm Hg versus 98.6 ± 1.34 mm Hg; $p < 0.05$). At the end of the operation, no significant differences were obtained (group 1, 98.7 ± 0.9 mm Hg, and group 2, 98.3 ± 1.7 mm Hg).

In both groups, a significant increase in PAP was observed after induction of anesthesia and onset of mechanical ventilation (group 1, 24.5 ± 5.8 to 42.5 ± 13.5 mm Hg; $p < 0.05$; group 2, 24.1 ± 4.9 to 29.0 ±

Table 2. Recipient Preoperative Right Heart Catheterization Data[a,b]

Variable	Group 1 (with ECC; n = 4)	Group 2 (no ECC; n = 19)
RAP (mm Hg)	4.3 ± 2.2	4.9 ± 3.3
PAP (mm Hg)	24.5 ± 5.8	24.1 ± 4.3
PCWP (mm Hg)	6.0 ± 3.2	6.0 ± 4.1
CI ($L \cdot min^{-1} \cdot m^{-2}$)	3.10 ± 0.10	2.70 ± 0.73
PVR (dyne s cm^{-5})	299 ± 82	331 ± 187
MAP (mm Hg)	87.0 ± 10.4	92.7 ± 10.8

[a] Data are shown as the mean ± the standard deviation. [b] There were no significant differences between groups for any of these variables.

CI = cardiac index; ECC = extracorporeal circulation; MAP = mean arterial pressure; PAP = mean pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RAP = right atrial pressure.

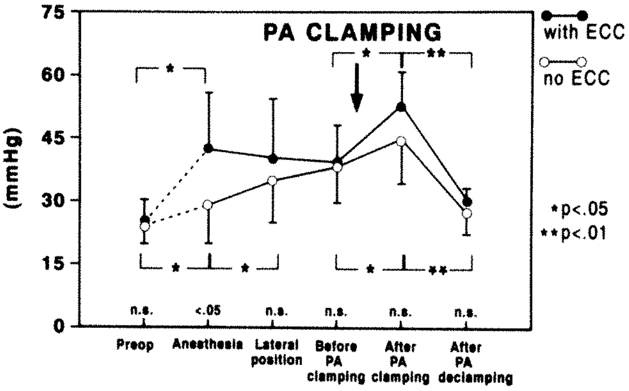


Fig 2. *Mean pulmonary artery pressure (mean ± standard deviation). Abbreviations are the same as in Figure 1.*

9.1 mm Hg; $p < 0.05$), and a further rise was noted in group 1 after the patient was placed in the lateral position (Fig 2). No significant differences were found after this maneuver (group 1, 40.5 ± 14.0 mm Hg, and group 2, 34.9 ± 10.1 mm Hg) and before PA clamping (group 1, 39.3 ± 8.9 mm Hg, and group 2, 38.2 ± 8.6 mm Hg). With clamping of the PA, a considerable rise in PAP was seen in both groups, but the differences between them were not significant (group 1, 53.3 ± 7.6 mm Hg, and group 2, 44.9 ± 10.7 mm Hg). After PA declamping, PAP normalized in both groups (group 1, 30.3 ± 2.9 mm Hg, and group 2, 27.4 ± 5.2 mm Hg; p = not significant).

Similar to PAP, the pulmonary capillary wedge pressure revealed a significant increase in both groups at induction of anesthesia (group 1, 6.0 ± 3.2 to 12.5 ± 5.8 mm Hg; $p < 0.05$; group 2, 6.0 ± 4.1 to 11.8 ± 5.6 mm Hg; $p < 0.01$) (Fig 3). A further rise was noted after lateral positioning of the patients in group 1, but the differences were not significant (group 1, 14.3 ± 4.0 mm Hg, and group 2, 11.8 ± 4.8 mm Hg). Clamping of the PA did not cause any significant alteration in pulmonary capillary wedge pressure between patients in each group or between groups (group 1, 16.3 ± 3.8 mm Hg, and group 2, 16.3 ± 6.9 mm Hg). After PA declamping, values decreased to those obtained at induction of anesthesia (group 1, 13.3 ± 4.1 mm Hg, and group 2, 11.9 ± 4.6 mm Hg). This decrease was significant in group 2 ($p < 0.05$) but not between groups.

Cardiac index was stable without any significant changes in either group before PA clamping (Fig 4). After occlusion of the PA, CI decreased approximately 1.5 $L \cdot min^{-1} \cdot m^{-2}$ in the 4 patients requiring ECC but remained stable in the remaining 19 patients (group 1, 3.02 ± 0.25 to 1.54 ± 0.46 $L \cdot min^{-1} \cdot m^{-2}$; $p < 0.01$; group 2, 2.71 ± 0.53 to 2.54 ± 0.41 $L \cdot min^{-1} \cdot m^{-2}$; p = not significant). This decrease in CI was highly significant in group 1, between the groups ($p < 0.01$), and also compared with the CI in group 1 before PA clamping (3.02 ± 0.25 $L \cdot min^{-1} \cdot m^{-2}$). During reperfusion, CI rose significantly in both groups (group 1, 1.54 ± 0.46 to 3.98 ± 1.04 $L \cdot min^{-1} \cdot m^{-2}$; $p < 0.01$; and group 2, 2.54 ± 0.41 to 3.18 ± 0.10 $L \cdot min^{-1} \cdot m^{-2}$; $p < 0.01$) because of catecholamine support in 3 of the 4 group 1 patients and 6 of the 19 patients of group 2.

Calculated PVR showed a comparable pattern without any significant changes before PA clamping (Fig 5). A significant rise was found after clamping of the PA in the 4 patients needing ECC, whereas PVR remained stable in group 2 (group 1, 434 ± 148 to 1,188 ± 235 dyne · s · cm^{-5};

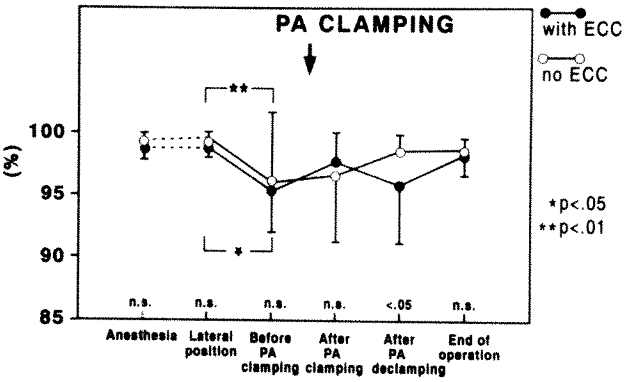


Fig 1. *Arterial oxygen saturation (mean ± standard deviation). (ECC = extracorporeal circulation;* n.s. *= not significant;* PA *= pulmonary artery.)*

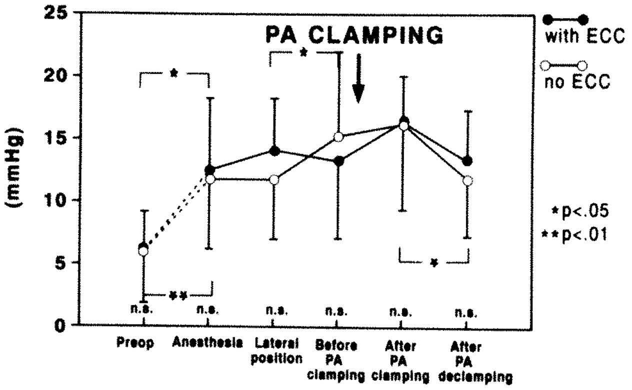


Fig 3. *Pulmonary capillary wedge pressure (mean ± standard deviation). Abbreviations are the same as in Figure 1.*

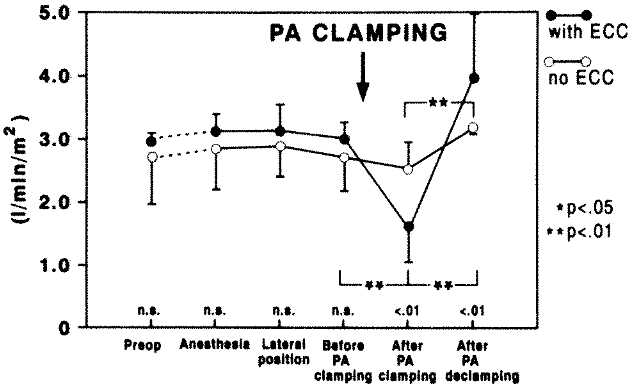


Fig 4. *Cardiac index (mean ± standard deviation). Abbreviations are the same as in Figure 1.*

$p < 0.01$; group 2, 395 ± 176 to 462 ± 197 dyne · s · cm^{-5}; p = not significant). This difference in PVR after PA clamping was highly significant ($p < 0.01$). After declamping, PVR values returned to normal uniformly (group 1, 189 ± 42 dyne · s · cm^{-5}, and group 2, 238 ± 141 dyne · s · cm^{-5}; p = not significant).

Comment

The first lung transplantation in a human was performed by Hardy and associates [17] in 1963. Since then, most problems related to surgical technique [6, 15, 18] and lung preservation [9, 19, 20] have been solved, as reflected by the increasing number of successful procedures [1]. However, extended indications and more demanding procedures are generating new problems concerning intraoperative and perioperative patient management. Although ECC is indispensable for graft implantation in heart-lung transplantation and en bloc double-lung transplantation, sequential double-lung transplantation and single-lung transplantation for idiopathic fibrosis or pulmonary emphysema are feasible without cardiopulmonary bypass in most cases [6, 15]. This is particularly important for patients with a previous thoracic procedure or pleural adhesions of other origin who are facing the risk of severe bleeding under full heparinization.

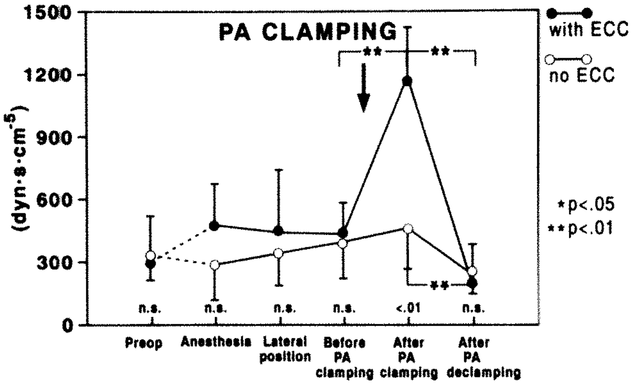


Fig 5. *Pulmonary vascular resistance (mean ± standard deviation). Abbreviations are the same as in Figure 1.*

However, no criteria have been established to predict the necessity of ECC during single-lung transplantation in patients with parenchymal lung disease. In choosing an adequate operative strategy, it would be desirable to have those criteria available preoperatively. In any case, the decision for or against the use of cardiopulmonary bypass must be made after occlusion of the PA. Once the lung has been removed, there is no way to reduce the afterload of a rapidly failing right ventricle, and cannulation for bypass may produce a real emergency.

Based on the results of this study, preoperative criteria aside from the intraoperative course of the patient can be considered in assessing the indication for cardiopulmonary bypass. In our experience, however, preoperative variables obtained at right heart catheterization were not useful. In particular, PAPs were only moderately elevated and CIs were similar in both groups without any significant differences. In addition, respiratory function tests were not predictive in patients with pulmonary fibrosis.

Intraoperative hemodynamics remained stable with only minor changes in both groups until the PA was clamped. Careful clamping of the PA and termination of the ipsilateral ventilation usually resulted in a similar increase in PAP in both groups within an acceptable range. In retrospect, this pattern alone was not helpful in deciding on the need of ECC, as its effects on right ventricular function varied considerably. The significant decrease in CI immediately after PA clamping in group 1, however, clearly reflected right ventricular deterioration. The simultaneous increase in PVR unequivocally demonstrated the serious afterload situation for the right ventricles. Under these conditions, ECC should be instituted to maintain stable hemodynamics if a brief trial (2 to 3 minutes) of catecholamines and nitrates does not work. If only a moderate decrease in CI with a slight increase in PVR is present, the operation can proceed with pharmacological support alone.

Our findings suggest that a decrease in CI of more than 1.5 L · min^{-1} · m^{-2} in adults represents the critical value for the need of ECC. Therefore, lung transplantation for parenchymal lung disease should be performed only by services familiar with the rapid institution of ECC, as the need for cardiopulmonary bypass may not be predictable on the basis of preoperative studies. Also, it became evident that the low vascular resistance of the transplanted lung allowed excellent right ventricular recovery during reperfusion, as reflected by normal PVR and CI values.

In the present series, frequent determination of CI and PVR values by thermodilution technique allowed an adequate estimation of right ventricular performance during graft implantation. This can be supplemented by monitoring the central venous saturation measured continuously in the PA by a fiberoptic technique. Intraoperative transesophageal echocardiography also allows continuous observation of right ventricular function as demonstrated by Simon and co-workers [21].

We conclude that preoperative cardiopulmonary criteria including right heart catheterization data as well as intraoperative hemodynamic measurements obtained before clamping the PA are not indicative of the need of ECC in patients undergoing single-lung transplantation for pulmonary fibrosis. Intraoperative assessment of CI and calculation of the PVR seem to be essential for assessing cardiac performance. A decrease in CI of more than 1.5 $L \cdot min^{-1} \cdot m^{-2}$ after PA occlusion is indicative of the need of ECC, whereas a rise in PAP alone does not reflect the degree of right ventricular failure.

References

1. Kriett JM, Kaye MP. The Registry of the International Society for Heart and Lung Transplantation: eighth official report—1991. J Heart Lung Transplant 1991;10:491–8.
2. Jamieson SW, Stinson EB, Oyer PE, et al. Heart-lung transplantation for irreversible pulmonary hypertension. Ann Thorac Surg 1984;38:554–62.
3. Patterson GA, Cooper JD, Dark JH, Jones MT, Toronto Lung Transplant Group. Experimental and clinical double lung transplantation. J Thorac Cardiovasc Surg 1988;95:70–4.
4. Reitz BA, Wallwork JL, Hunt SA, et al. Heart-lung transplantation: successful therapy for patients with pulmonary vascular diseases. N Engl J Med 1982;306:557–63.
5. McGregor CGA, Dark JH, Hilton CJ, Freeman R, Conacher ID, Corris PA. Early results of single lung transplantation in patients with endstage pulmonary fibrosis. J Thorac Cardiovasc Surg 1989;98:350–4.
6. Noirclerc M, Metras D, Vaillant A, et al. Technique chirurgicale de la transplantation bipulmonaire. Lyon Chir 1989;85: 247–51.
7. Braunwald E. Heart diseases. 3rd ed. Philadelphia: Saunders, 1988:257.
8. Wahlers T, Schäfers HJ, Cremer J, et al. Organ preservation for heart-lung and lung transplantation. Thorac Cardiovasc Surg 1991;39:344–8.
9. Haverich A, Aziz S, Scott WC, Jamieson SW, Shumway NE. Improved lung preservation using Euro-Collins solution for flush perfusion. Thorac Cardiovasc Surg 1986;34:368–76.
10. Stuart RS, Monte S, Baumgartner WA, et al. Successful 4 hour hypothermic lung storage with Euro-Collins solution: a simplified model assessing preservation. Heart Transplant 1984;3:346–51.
11. Haverich A, Wahlers T, Schäfers HJ, et al. Distant organ procurement in clinical lung- and heart-lung transplantation. Eur J Cardio-thorac Surg 1990;4:245–9.
12. Jurmann MJ, Dammenhayn L, Schäfers HJ, Wahlers T, Fieguth HG, Haverich A. Prostacyclin as an additive to single crystalloid flush. Improved pulmonary preservation in heart-lung transplantation. Transplant Proc 1987;19:4103–4.
13. Lehtola A, Harjula A, Heikkila L, et al. Single-lung allotransplantation in pigs following donor pretreatment with intravenous prostaglandin E-1. Scand J Thorac Cardiovasc Surg 1989;23:193–9.
14. Todd TR, Goldberg M, Koshal A, et al. Separate extraction of cardiac and pulmonary grafts from a single organ donor. Ann Thorac Surg 1988;46:356–9.
15. Cooper JD, Pearson FG, Patterson GA, et al. Technique of successful lung transplantation in humans. J Thorac Cardiovasc Surg 1987;93:173–81.
16. Brosius G. SPSS, PC+ advanced statistics and tables. New York: McGraw-Hill, 1989.
17. Hardy JD, Webb WR, Dalton ML, Walker GR. Lung homotransplantation in man. JAMA 1963;186:99–108.
18. Patterson GA, Cooper JD, Goldman B, et al. Technique of successful clinical double-lung transplantation. Ann Thorac Surg 1988;45:626–33.
19. Wahlers T, Haverich A, Fieguth HG, Schäfers HJ, Takayama T, Borst HG. Flush perfusion using Euro-Collins solution vs cooling by means of extracorporeal circulation in heart-lung preservation. J Heart Transplant 1986;5:89–98.
20. Locke TJ, Hooper TL, Flecknell PA, et al. Preservation of the lung: comparison of flush perfusion with cold modified blood and core cooling by cardiopulmonary bypass. J Heart Lung Transplant 1991;10:1–8.
21. Simon P, Jellinek H, Hiesmayer H, Mohl W, Laczkovics A, Klepetko W. Intraoperative transösophageale Echocardiographie zum Monitoring der Rechtsventrikelfunktion während Lungentransplantation. Atemwegs- und Lungenerkrankungen 1991;17(Suppl):17.

DISCUSSION

DR PETER P. McKEOWN (Tampa, FL): I compliment Dr Hirt and associates on an excellent presentation. I wonder if perhaps there are not some features that you overlooked in the preoperative assessment, such as resting oxygenation or first-pass multigated acquisition, right and left ventricular ejection fractions, or standard angiographic techniques. I also wonder if there was any difference between the right and left sides.

DR HIRT: It is difficult to compare preoperative oxygenation data between these patients because of their different dependency on oxygen. However, the ratio of partial pressure of oxygen to inspired oxygen fraction after the onset of artificial ventilation was similar in both groups without significant differences. The right and left ventricular ejection fractions were not obtained preoperatively in all patients studied. Especially in the younger patients ventricular function was assessed by echocardiography aside from measurement of filling pressures and cardiac output using thermodilution techniques. For this reason, we did not compare right and left ventricular ejection fractions in the study groups.

DR BARTLEY P. GRIFFITH (Pittsburgh, PA): Dr Hirt, my question is similar to the last one. In nonvascular disease of the lung, it is our experience that the usual problems intraoperatively are hypoxia or hypercarbemia. Do you have a prescription for which patients preoperatively might be those who would require extracorporeal circulation intraoperatively not so much to assist the cardiac index but to have adequate gas exchange?

DR HIRT: In our experience, no desaturation or hypercarbemia occurred in these patients with the underlying diagnosis of pulmonary fibrosis. It is, however, a common feature in candidates with pulmonary obstructive disease. We think that monitoring gas exchange is not sensitive enough to predict the necessity of extracorporeal circulation in lung transplantation for restrictive lung disorders. In the patient group requiring institution of bypass, oxygenation was still excellent after the clamping of the pulmonary artery, but right ventricular failure, reflected by a significant decrease in cardiac index, was evident.

DR GRIFFITH: Did you persist in any of the patients with a low cardiac index before the use of extracorporeal circulation? In spite of a drop in cardiac output, did you try to get by without the use of extracorporeal circulation in any patient?

DR HIRT: Extracorporeal circulation was instituted only if maximal vasodilator and catecholamine support was unable to stabilize the circulation.

Stentless Porcine and Pericardial Valve in Aortic Position

Riccardo Casabona, MD, Ruggero De Paulis, MD, Giuseppe F. Zattera, MD,
Michele di Summa, MD, Walter Bottone, MD, Carla Stacchino, MD,
Mario O. P. Vrandecic, MD, and Mario Morea, MD

Cardiac Surgery Department, University of Torino, Torino, Italy, and Belo Horizonte, Brazil

Fifty-seven patients underwent aortic valve replacement with a stentless glutaraldehyde-fixed bioprosthesis; 27 received a porcine aortic valve and 30 had a bovine pericardial valve. Two groups of 30 patients each who had aortic valve replacement with a tilting-disc mechanical valve or a stented porcine bioprosthesis served as controls. There were no differences in sex, body surface area, valve lesion, and valve size among the four groups. Results were assessed on a Doppler-based determination of maximum velocity across the valve, aortic valve area, and degree of valve regurgitation. Velocity across the valve was significantly less with stentless pericardial valves than with stentless porcine valves, stented bioprostheses, and mechanical valves. Stentless valves had a significantly larger aortic valve area when compared with stented valves. Mild central aortic insufficiency was detected more often with stentless pericardial than with stentless porcine bioprostheses ($p = 0.04$). Stentless valves showed a higher incidence of complete atrioventricular block when compared with stented valves ($p = 0.04$). Long-term studies are now warranted to assess the durability of both types of stentless valves.

(Ann Thorac Surg 1992;54:681–5)

Whenever replacing an aortic valve with a biological or a mechanical heart prosthesis we leave gradients that could be quite unacceptable, especially in the small aortic annulus [1]. In this case, although the results with some of the currently available mechanical valves might be quite satisfactory, a porcine valve almost always will be a poor choice [2, 3]. There is evidence that in the small sizes the level of valvular obstruction is lower with pericardial valves than with porcine valves [4, 5]. Even though improvement in valve material and valve design have optimized the hemodynamic characteristics of heart valve prostheses in recent years [6], the presence of a more or less cumbersome stent will always result in a serious degree of obstruction. Selection of a prosthesis with a good hemodynamic profile might be of substantial importance. Therefore, aortic allograft valves have been used because of their good hemodynamic characteristics [7]. However, an important limitation of this type of valve is the lack of adequate donors.

After promising experimental results using a stentless porcine valve in sheep [8], David and colleagues started a controlled clinical trial [9] several years after the first pioneering experiences [10, 11].

Encouraged by the positive hemodynamic results being reported, we started a clinical trial using two types of commercially available stentless valve: a pericardial valve and a porcine valve. Their results were analyzed and compared with those of two groups of patients receiving a mechanical or a porcine stented valve.

Material and Methods

Stentless Porcine Aortic Valve

This valve was manufactured by Biocor Industria e Pesquisa Ltda, Belo Horizonte, MG, Brazil. Its specifications are based on the selection of individual porcine cusps to mount a composite bioprosthesis, avoiding leaflets with muscular bands. The leaflets are treated under no pressure and are tanned with different glutaraldehyde solutions for a period of 3 months. The leaflets are sutured to a conduit of glutaraldehyde-treated bovine pericardium using a 5-0 Mersilene suture. The conduit is then shaped in a scalloped manner to mimic the natural aortic valve.

Stentless Pericardial Aortic Valve

This valve was manufactured by Sorin Biomedica, Saluggia, Italy. It is made of two separate sheets of glutaraldehyde-treated bovine pericardium. The first sheet is shaped to form the three leaflets by means of a process of atraumatic tissue fixation without the use of molds. It is then sutured to the second sheet using a pyrolite carbon-coated suture. The suture line is especially designed to dampen the mechanical stress at the level of the commissures.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Dr De Paulis' present address is Cardiac Surgery Department, II University of Rome, Rome, Italy.

Address reprint requests to Dr Morea, Cattedra di Cardiochirurgia, C.so Polonia 14, 10126 Torino, Italy.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Stented Porcine and Mechanical Valves

The porcine valve that served as control was the Biocor stented bioprosthesis manufactured by Biocor Industria e Pesquisa Ltda with specifications similar to those described for the stentless valves but sutured to a Dacron-covered flexible stent. The mechanical valve was the Omnicarbon valve, manufactured by Medical Inc, Inver-Grove Heights, Minnesota, which is the third-generation valve of the Lillehei-Kaster prosthesis with the titanium housing being replaced with a carbon-coated housing to reduce the potential for thromboembolic complications.

Patients and Procedure

Fifty-seven consecutive patients underwent isolated aortic valve replacement with a glutaraldehyde-fixed stentless aortic valve; 27 received a porcine valve and 30 a pericardial valve. Two groups of 30 patients each who received a stented bioprosthesis or a mechanical valve served as control. Patients with associated procedures were excluded. The age distribution among the four groups of patients was slightly different, with the stentless porcine and the mechanical valve patients being younger (mean, 50.2 ± 15.5 and 49 ± 14.6 years) than the patients with stentless pericardial valves (61.1 ± 14.3 years) or the standard bioprostheses (63.1 ± 7.5 years) ($p < 0.05$). There were no differences in sex distribution, preoperative diagnosis, or body surface area. Furthermore, prosthetic valve size, although not perfectly matched, was evenly distributed among the four groups (p = not significant). The majority of patients (107/117; 91.4%) were in sinus rhythm; none had complete heart block.

The stentless valves were sutured in place as follows: the lower suture was done in a continuous manner using a 4-0 polypropylene suture with care being taken at the level of the atrioventricular node, where the suture was slightly higher on the annular fibrous tissue. The second layer of the suture was always done with a continuous 4-0 polypropylene suture.

All patients underwent transthoracic echocardiographic study a few days after operation and at 3, 6, and 12 months postoperatively. The maximum velocity across the valve was measured by continuous-wave Doppler echocardiography, the aortic valve area was calculated with the continuity equation [12], and color Doppler echocardiography with pulse wave mapping technique [7] was used for detection of prosthetic valve regurgitation. The follow-up was 9 ± 4 months (range, 3 to 17 months) for the stentless porcine valve, 14 ± 5 months (range, 5 to 22 months) for the stentless pericardial valve, 17 ± 7 months (range, 7 to 27 months) for the stented Biocor valve, and 29 ± 12 months (range, 9 to 42 months) for the Omnicarbon valve. Because the mechanical valves had a longer follow-up, we considered only the echocardiographic evaluation done at 6 and 12 months after the operation.

All values are expressed as mean ± standard deviation. Continuous variables were compared by analysis of variance, and noncontinuous variables were compared by the χ^2 test. A p value less than 0.05 was defined as statistically significant.

Table 1. Comparison of Hemodynamic Data Among the Four Groups of Patients[a]

Prosthesis	No. of Patients	V_{max} (m/s)	AVA (cm^2)
Stentless porcine	27	1.98 ± 0.4	1.83 ± 0.3
Stentless pericardial	30	1.82 ± 0.4	1.72 ± 0.2
Stented Biocor	30	2.29 ± 0.3[b]	1.56 ± 0.1[b]
Omnicarbon	30	2.54 ± 0.6[b]	1.38 ± 0.1[b]

[a] Values are expressed as mean ± standard deviation of the mean. [b] $p < 0.05$ versus both stentless valves.

AVA = aortic valve area; V_{max} = maximum velocity across the valve.

Results

Three patients (11.1%) who received a stentless porcine valve died within 30 days after operation. The first one had a complete atrioventricular block and malfunctioning of the temporary pacemaker, and the other 2 died because of respiratory insufficiency due to a severe primary pulmonary disease. One patient (3.3%) who received a stentless pericardial valve had a sudden death 6 months after operation. One patient (3.3%) in the Omnicarbon group died because of an anticoagulation-related hemorrhage 2 years after operation, and another 1 had a nonfatal thromboembolic complication 6 month after operation. One patient in the stented Biocor group (3.3%) and 1 patient in the Omnicarbon group (3.3%) underwent reoperation for periprosthetic dehiscence at an interval of 8 and 10 months after operation. The remaining patients had an uneventful postoperative course without thromboembolic events or infective endocarditis. None of the patients with stentless valve received anticoagulation therapy. Patient with the stented Biocor valve were anticoagulated for the first 3 months postoperatively. Patients with mechanical valves received lifelong anticoagulation drugs. All patients had symptomatic improvement: 83.3% and 69.3% of patients with stentless porcine and pericardial valves were in New York Heart Association class I as were 81.5% and 74.1% of patients with a stented Biocor and Omnicarbon valve, respectively; the remaining patients were in class II.

Stentless valves showed an higher incidence of atrioventricular block (5 cases in the stentless porcine group and 1 case in the stentless pericardial group) when compared with stented valves (1 case in the Biocor group and none in the Omnicarbon group) ($p = 0.04$). The lowest maximum velocity across the valve was found in patients with stentless pericardial valves. Maximum velocity across the valve was significantly lower with stentless pericardial valves and stentless porcine valves than with stented Biocor or Omnicarbon valves (Table 1). This trend was confirmed for each valve size, with data being statistically significant for the smaller valve sizes ($p < 0.05$ for the No. 23 and 25) (Table 2). Accordingly, aortic valve areas were significantly larger with stentless valves when

Table 2. Comparison of Hemodynamic Data for Each Valve Size Among the Four Groups of Patients[a]

Valve Size	Prosthesis	No. of Patients	BSA (cm^2)	V_{max} (m/s)	AVA (cm^2)
23	Stentless porcine	5	161.8 ± 5.4	2.22 ± 0.6	1.59 ± 0.3
	Stentless pericardial	8	159.7 ± 7.9	1.93 ± 0.3	1.50 ± 0.06
	Stented Biocor	8	164.6 ± 7.9	2.47 ± 0.2[b]	1.40 ± 0.05[c]
	Omnicarbon	8	173.7 ± 16.9	2.72 ± 0.1[b]	1.44 ± 0.1
25	Stentless porcine	10	165.9 ± 12	1.91 ± 0.3	1.76 ± 0.3
	Stentless pericardial	5	175.3 ± 22.3	1.85 ± 0.3	1.63 ± 0.1
	Stented Biocor	16	170.4 ± 12.5	2.30 ± 0.3[b]	1.58 ± 0.1[c]
	Omnicarbon	15	176.6 ± 12.4	2.40 ± 0.6[b]	1.35 ± 0.1[b]
27	Stentless porcine	5	173.2 ± 3.1	1.98 ± 0.4	1.76 ± 0.04
	Stentless pericardial	8	184.8 ± 12.9	1.86 ± 0.5	1.77 ± 0.1
	Stented Biocor	3	177.6 ± 9.2	2.23 ± 0.2	1.60 ± 0.1
	Omnicarbon	5	186.8 ± 9.3	2.40 ± 0.7	1.40 ± 0.1[b]
29	Stentless porcine	6	186.5 ± 13.3	1.80 ± 0.1	2.20 ± 0.4
	Stentless pericardial	7	170.5 ± 14.3	1.55 ± 0.5	1.99 ± 0.4
	Stented Biocor	3	170.6 ± 23.4	1.80 ± 0.1	1.88 ± 0.04
	Omnicarbon	1	201	2.2	1.52

[a] Values are expressed as mean ± standard deviation. [b] $p < 0.05$ versus both stentless valves. [c] $p < 0.05$ versus stentless porcine valve.

AVA = aortic valve area; BSA = body surface area; V_{max} = maximum velocity across the valve.

compared with stented ones ($p < 0.05$) (see Table 1). The results were confirmed for each valve size, with data being statistically significant in the smaller valve sizes (see Table 2). No significant differences were found within the two groups of stentless valves. Cardiac outputs obtained by the Doppler echocardiographic technique were similar among the four groups of patients and correlated well with body surface areas.

Color Doppler echocardiography revealed trivial or mild central aortic regurgitation in 18 stentless valves (31.6%). This finding was more common with stentless pericardial prostheses (13 cases, 43.3%) than with stentless porcine (5 cases, 18.5%), and the difference was statistically significant ($p = 0.04$). The difference was more evident for the No. 23 valve size: 7/8 (87.5%) versus 2/8 (20%), respectively ($p = 0.01$). Nevertheless, none of these patients was symptomatic.

Comment

Stentless aortic valves will obviously be more difficult to implant when compared with standard bioprostheses or mechanical valves. An optimal result will more often be reliant on the surgeon's skill. Misjudgment in the commissure positioning and alignment in the aortic root or in the choice of the valve size will result in an incompetent prosthesis. However, as is true for stented porcine and pericardial valves, the hemodynamic performances of stentless valves might also depend on the type of valve and on the tissue employed. This study shows that pericardial valves have a higher incidence of central aortic insufficiency when compared with similar porcine valves. Although this insufficiency is almost always trivial or mild and has no consequences for the patients' clinical status, still it deserves some discussion. It could depend on a more difficult sizing and positioning of the pericardial valve and could therefore be related to the surgeon's experience. This is further confirmed by the fact that the insufficiency was more often detected in smaller sized valves, which can be more difficult to implant. Hopefully, as the surgeon's confidence with this type of valve increases, the results will improve accordingly. On the other hand, the incompetence could be due to the particular stiffness of the pericardial tissue, which requires a higher closing volume and a consequent higher regurgitation volume. In this case the stretching of the pericardial leaflets after implantation could result in a moderate degree of cusp extension, which will partially compensate for this problem.

The higher occurrence of complete atrioventricular block in patients with stentless valves is probably due to the surgical technique of implantation and therefore related to the surgeon's learning curve. Proximal interrupted or semicontinuous sutures should probably be preferred to a continuous running suture, which could result in a pursestring effect.

The elimination of the stent, which would allow the implantation of a valve with a larger effective orifice area for a given aortic diameter, will obviously result in better hemodynamic performances. From this point of view the results are expected to be similar to those with autologous pulmonary valve [13] and fresh and frozen preserved homograft [14, 15].

Lately, there has been renewed interest in the use of stentless bioprostheses [9, 16]. Some authors [16] found this valve particularly applicable in the small aortic annulus, avoiding annulus enlargement; in cases of active endocarditis, to minimize the amount of foreign material; and when long-term anticoagulation is contraindicated. Furthermore, its use has been reported in particular anatomical settings such as the presence of an aneurysm of the sinuses of Valsalva [17]. Overall, the primary justification for the use of this type of valve is based on the improved durability that should be achieved by using the aortic wall as a valve stent.

Once stentless valves are implanted, the anatomy of the outflow tract appears identical to that of patients with a natural valve. Therefore, we can rely on the validity of the Doppler echocardiography in the assessment of valve function. Furthermore, earlier studies demonstrated the accuracy of aortic bioprosthetic valve pressure gradients measurements in comparing groups of patients with bioprosthetic valves [18]. Recently Rothbart and associates [19] convincingly demonstrated the validity of applying the Doppler continuity equation to bioprosthetic aortic valves. On the other hand, because of more complex fluid dynamics, the same assumption might not be true in the case of mechanical valves [20].

The present study clearly shows that stentless valves offer a significantly lower gradient when compared with either biological stented valves or mechanical valves. Although this trend was evident for each valve size, it was more significant in the smaller sizes (see Table 2). Similarly, the aortic valve areas were larger in patients with stentless valves than in patients with stented valves even though the difference did not reach statistical significance for every valve size (see Table 2). As would have been expected, the hemodynamic advantages become evident with the decrease in valve size. Jaffe and colleagues [21] used Doppler echocardiography to measure gradients and valve areas in patients with small allografts, Medtronic Intact porcine bioprostheses, and St. Jude Medical mechanical valves. They found that gradients across the allografts and the majority of St. Jude valves were low when compared with stented porcine valves. However, in our study the hemodynamic profile of stentless valves was superior to both stented bioprostheses and mechanical valves. This could be explained by the known better hemodynamics of the St. Jude Medical valve when compared with a tilting-disc valve [3] and by the limitation of the Doppler echocardiographic evaluation in patients with mechanical valves [20].

There are no clear differences and therefore no substantial advantages that may justify the use of one type of stentless valve over the other. Both are clearly superior to stented bioprostheses and become the first choice when a tissue valve is indicated and the patient has a small aortic annulus. Optimization of the surgical technique is required to avoid prosthetic valve regurgitation and complete atrioventricular block. Time will be needed to see which material will afford better durability using the aortic wall as a valve stent.

We are thankful to Dr Carlo Bassano for the help in editing the manuscript.

References

1. David TE, Uden DE. Aortic valve replacement in adult patients with small aortic annuli. Ann Thorac Surg 1983;36:577–83.
2. Gray RJ, Chaux A, Matloff JM, et al. Bileaflet, tilting disc and porcine aortic valve substitutes: in vivo hydrodynamic characteristics. J Am Coll Cardiol 1984;3:321–7.
3. Panidis IP, Ross J, Mintz GS. Normal and abnormal prosthetic valve function as assessed by Doppler echocardiography. J Am Coll Cardiol 1986;8:317–26.
4. Cosgrove DM, Lytle BW, Gill CC, et al. In vivo hemodynamic comparison of porcine and pericardial valves. J Thorac Cardiovasc Surg 1985;89:358–68.
5. Rashtian MY, Stevenson DM, Allen DT, et al. Flow characteristics of bioprosthetic heart valves. Chest 1990;98:365–75.
6. Carpentier A, Dubost C, Lane E. Continuing improvement in valvular prostheses. J Thorac Cardiovasc Surg 1982;83:27–42.
7. Jaffe WM, Coverdale A, Roche AHG, Brandt PWT, Ormiston JA, Barratt-Boyes BG. Doppler echocardiography in the assessment of the homograft aortic valve. Am J Cardiol 1989;63:1466–70.
8. David TE, Ropchan GC, Butany JW. Aortic valve replacement with stentless porcine bioprostheses. J Cardiac Surg 1988;3:501–5.
9. David TE, Pollick C, Bos J. Aortic valve replacement with stentless porcine aortic bioprostheses. J Thorac Cardiovasc Surg 1990;99:113–8.
10. Binet JP, Duran CG, Carpentier A, Langlois J. Heterologous aortic valve transplantation. Lancet 1965;2:1275.
11. O'Brien MF, Clarebrough JK. Heterograft aortic valve transplantation for human valve disease. Med J Aust 1966;2:228–30.
12. Teirstein P, Yeager M, Yock PG, Popp RL. Doppler echocardiographic measurements of aortic valve area in aortic stenosis: a noninvasive application of the Gorlin formula. JACC 1986;8:1059–65.
13. Gula G, Wain WH, Ross DN. Ten years' experience with pulmonary autograft replacements for aortic valve disease. Ann Thorac Surg 1979;28:392–6.
14. Penta A, Qureschi S, Radley-Smith R, Yacoub MH. Patient status 10 or more years after "fresh" homograft replacement of the aortic valve. Circulation 1984;70:182–6.
15. Ross DN, Yacoub MH. Homograft replacement of the aortic valve. A critical review. Prog Cardiovasc Dis 1969;9:275–9.
16. Vilela Batista RJ, Dobrianskij A, Comazzi M, et al. Clinical experience with stentless pericardial aortic monopatch for aortic valve replacement. J Thorac Cardiovasc Surg 1987;93:19–26.
17. Sievers HH, Podszus G, Lange PE, Bursch JH, Bernard A. Replacement of the aortic root by free implantation of a stentless aortic porcine bioprosthesis in a patient with aneurysm of the sinuses of Valsalva. J Thorac Cardiovasc Surg 1985;33:360–1.
18. Reisner SA, Meltzer RS. Normal values of prosthetic valve Doppler echocardiographic parameters: a review. J Am Soc Echo 1988;1:201–10.
19. Rothbart RM, Castriz JL, Harding LV, Russo CD, Teague SM. Determination of aortic valve area by two-dimensional and Doppler echocardiography in patients with normal and stenotic bioprosthetic valves. J Am Coll Cardiol 1990;15:817–24.
20. Otto CM, Pearlman AS. Doppler echocardiography evaluation of stenotic bioprosthetic aortic valves. J Am Coll Cardiol 1990;15:825–6.
21. Jaffe WM, Coverdale A, Roche AHG, Whitlock RML, Neutze JM, Barrat-Boyes BG. Rest and exercise hemodynamics of 20 to 23 mm allograft, Medtronic Intact (porcine), and St. Jude Medical valves in the aortic position. J Thorac Cardiovasc Surg 1990;100:167–74.

DISCUSSION

MR ENDRE BODNAR (Pinner, United Kingdom): I have three questions. First, how did you detect regurgitation in these valves; what method did you use?

DR DE PAULIS: The insufficiency was detected by color Doppler echocardiography using the method of pulse-wave mapping technique, in which you put the sample volume in several places below the aortic valve.

When I said trivial regurgitation I meant that the regurgitant flow was detected just a few millimeters below the aortic ring, and when I said mild the regurgitant flow was detected inside the left ventricular outflow tract.

MR BODNAR: Well, that was going to be my second question, whether you attempted to quantify the regurgitation.

Third, taken that regurgitation is a fairly constant phenomenon with these valves, did you try to measure hemolysis, and if you did, what is the hemolysis like with these valves?

DR DE PAULIS: We did not quantify the hemolysis, but apparently we did not have any problems.

DR D. CRAIG MILLER (Stanford, CA): Could you translate the maximum velocity values to aortic valve areas for us?

DR DE PAULIS: I used maximum velocity because it is just the number we are actually measuring. Because of the Bernoulli equation the square of this number has to be multiplied by 4. Therefore, 2 m/s means a gradient of 16 mm Hg. Between a maximum velocity of 2 and 3 m/s we go from 16 to 36 mm Hg of gradient.

DR MILLER: But did you go one step further and measure the diameter of the left ventricular outflow tract and derive an estimated aortic valve area for the four types of valves?

DR DE PAULIS: Yes. This was done with the continuity equation, in which you need to measure the velocity in the outflow tract and at the level of the aortic valve and then you measure the diameter of the left ventricular outflow tract. However, there is some evidence in the literature showing that sometimes the measurement of the outflow tract could be avoided.

DR MILLER: Maybe I missed it. Did you report the aortic valve area data?

DR DE PAULIS: Yes.

DR MILLER: Then I did miss it. I apologize. I noted there was no substantial difference in hemodynamics between the stented porcine valve and the tilting-disk mechanical valve. Would you care to comment about that?

DR DE PAULIS: The main reason is that in the tilting-disk mechanical valves the accuracy of the Doppler echocardiographic evaluation is not well established because there is a difficulty in positioning the Doppler in the place where there is the maximum velocity. So that may be a bias of the study. However, these data are not much different from those I found in the literature, where a maximum velocity of 2.3, 2.6, and 3.3 m/s has been reported for the St. Jude mechanical valve, the Björk-Shiley valve, and the Starr-Edwards ball valve, respectively.

DR AURELIO CHAUX (Los Angeles, CA): Dr De Paulis, could you please tell us how long the follow-up was?

DR DE PAULIS: The follow-up is around 12 months for the stentless valves and for the stented bioprosthesis. It was a little longer, around 2 years, for the Omnicarbon valves.

DR CHAUX: Have you seen any change in the degree of regurgitation during this period of time?

DR DE PAULIS: No, actually it was pretty stable. In all of the Doppler examinations done a few days after and every 6 months, the amount of regurgitation stayed the same. Sometimes it decreased slightly.

Transhiatal Esophagectomy: A Safe Alternative for Selected Patients

Thomas M. Daniel, MD, Kirk J. Fleischer, MD, Terry L. Flanagan, MPH,
Curtis G. Tribble, MD, and Irving L. Kron, MD

Department of Surgery, University of Virginia Health Sciences Center, Charlottesville, Virginia

One hundred one consecutive patients underwent an esophagectomy with gastric interposition for benign and malignant processes from January 1982 through July 1990. Seventy-seven underwent transhiatal esophagectomy and 24, transthoracic esophagectomy. Multivariate analysis was performed comparing the hospitalization experience of the two groups. There was no significant difference found between the mean intraoperative blood loss for transhiatal esophagectomy (770 ± 105 mL) and that of transthoracic esophagectomy (700 ± 175 mL). There was a significant difference between operative time, with transhiatal esophagectomy averaging 5.4 hours and transthoracic esophagectomy averaging 7.3 hours. Postoperative stay was not significantly different although there was a wide range of values for the transthoracic esophagectomy group. An 8% operative mortality was experienced by both groups. There were a significant number of minor anastomotic leaks at the cervical anastomotic level for the transhiatal esophagectomy group, but all responded to nonoperative management. The highest morbidity and mortality were seen in the subgroup of transhiatal esophagectomies done for laryngocervical malignancies. The lowest morbidity and mortality were seen in the subgroup of 12 patients who underwent transhiatal esophagectomy for nonmalignant esophageal conditions. Transhiatal esophagectomy appears to be a safe alternative for early intrathoracic esophageal malignancies at any level, for bulky distal esophageal lesions, and for benign conditions requiring total esophagectomy.

(Ann Thorac Surg 1992;54:686–90)

Fourteen years have passed since Orringer and Sloan [1] rekindled interest in this country in using the transhiatal route for removing the esophagus. There have been multiple subsequent reports comparing transhiatal esophagectomy (THE) to transthoracic esophagectomy (TTE) addressing such issues as case selection [2], long-term survival [3], and immediate operative morbidity and mortality [4, 5]. The number of patients undergoing THE in these reports have been small, Hankins and associates [5] reporting 25 cases, Fok and colleagues [3] 38, and Goldfaden and co-workers [4] 29.

The focus of the present study was on the intraoperative and immediate postoperative characteristics of THE and TTE and not on their ultimate effectiveness in treating the underlying malignancy. The purpose of this study was to try to answer the following questions: (1) Was THE associated with a higher average blood loss than TTE? (2) Did THE require less operative time and cause less morbidity than TTE? (3) Was there a difference in the morbidity and mortality for THE done for malignant lesions at different levels of the proximal digestive tract?

Material and Methods

From January 1982 to July 1990, 101 consecutive patients underwent esophagectomy with gastric interposition for benign and malignant processes at the University of Virginia Health Sciences Center. Seventy-seven patients underwent THE and 24 underwent TTE. All charts were reviewed for age, operation, sex, tumor type and location, benign diagnosis when present, blood loss, length of operation, time to discharge, mortality, anastomotic leaks, and other less common complications.

Tumor location was defined as laryngocervical if the lesion lay between the larynx and 18 cm from the incisors. This level was considered to end at the thoracic inlet. The location was considered to be upper thoracic if the proximal extent of the tumor began between 19 and 29 cm from the incisors. The latter level corresponded to the inferior pulmonary veins. Lower thoracic lesions were defined as those whose proximal extent lay between 30 and 40 cm from the incisors. Operative mortality was defined in the study as any death occurring during the patient's operation or during the postoperative hospitalization period. Six of the eight deaths occurred within 30 days of operation. The remaining two deaths occurred 40 days and 70 days after operation.

Continuous data between more than two groups were compared using analysis of variance with Duncan's multiple range test. The frequency data were compared using χ^2 analysis. Significance was considered achieved when a p value of less than 0.05 was obtained.

Transhiatal esophagectomy was performed using an oblique left neck incision and an upper midline abdominal incision. A gastric pedicle was created, and a pyloromy-

---

Presented at the Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, FL, Nov 7–9, 1991.

Address reprint requests to Dr Daniel, Box 181, Department of Surgery, University of Virginia Health Sciences Center, Charlottesville, VA 22908.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Intraoperative and Postoperative Comparison of Transhiatal Esophagectomy and Transthoracic Esophagectomy[a]

Variable	THE	TTE	*p* Value
No. of Patients	77	24	
Intraoperative blood loss (mL)	770 ± 105	700 ± 175	NS
Operative time (h)	5.4 ± 0.3	7.3 ± 0.5	0.0017
Postoperative hospital stay (days)	22.4 ± 3.3	37.9 ± 18.1	NS
Operative mortality	6 (8%)	2 (8%)	

[a] Where applicable, values are shown as mean ± standard error of the mean.

NS = not significant; THE = transhiatal esophagectomy; TTE = transthoracic esophagectomy.

otomy or pyloroplasty was routinely done. The diaphragm was incised anteriorly at the esophageal hiatus just enough to admit the operator's hand. The esophagus was circumferentially freed up, working from the thoracic inlet and the abdomen, and after its removal the gastric pedicle was brought up through the esophageal bed. A single-layer cervical esophagogastric anastomosis was performed with interrupted synthetic monofilament absorbable suture after the stomach was fixed to the precervical fascia with several sutures. Chest tubes were only placed if the pleural space was entered during the dissection.

Transthoracic esophagectomy was performed using the same abdominal procedure as in THE. If there was a preoperative question of tumor fixation to the trachea or aorta, the neck incision was deferred until the transabdominal dissection determined whether a THE would be attempted. The thoracic incision was placed through the right sixth interspace. The esophagus was dissected out and the esophagogastric anastomosis placed as far cephalad as possible using an end-to-end anastomotic stapler passed through a small gastrotomy. A right chest tube was routinely placed.

Results

Seventy-seven male and 24 female patients underwent esophagectomy during the 8½-year study. The average age was 59.9 years. Resection was performed for 12 benign lesions and 89 malignant lesions. Of the malignant lesions 58 were squamous cell carcinomas and 31 were adenocarcinomas.

Operative Data

Over the course of the study the patients undergoing either THE or TTE had varying preoperative experiences ranging from preoperative radiation therapy only, to preoperative radiation therapy and chemotherapy, to no prior treatment with any other modality. Operative blood loss for both types of esophagectomy was found to be similar. Transhiatal esophagectomy averaged 770 mL loss and TTE, 700 mL loss (Table 1). Two episodes of massive bleeding occurred in the THE series. One patient recovered after a thoracotomy, which was required for control of the bleeding, and was subsequently discharged on the 30th postoperative day. The second patient died on the 5th postoperative day of further complications that followed the bleeding episode.

Operative time was found to be significantly different between the two procedures, with THE averaging 5.4 hours and TTE averaging 7.3 hours (see Table 1). Only 2 of the 24 TTEs represented cases where THE was attempted and converted to TTE. The length of these two operations fell within the mean of the TTE group and did not therefore affect the overall average time of that operation compared with the THE group.

Although the mean postoperative stay for THE was shorter than for TTE, it was not found to be significantly different because a wide range of values prevented meaningful comparison for the number of patients involved (see Table 1). The overall mean postoperative stay for THE for the entire study was 22.4 days. Increasing operative experience and case selection resulted in a mean postoperative stay of 15 days for the THE patients for the last 2 years of the study.

Mortality

Operative mortality for both groups was 8%. The causes of death after THE included respiratory insufficiency (3 patients), postoperative sequelae of tracheal injury (2), and postoperative sequelae of massive bleeding (1). All three of the bleeding and tracheal injury deaths occurred in the first 3 years of the study and in patients with laryngocervical tumors that had received preoperative radiation therapy. The two deaths after TTE were both due to respiratory insufficiency and subsequent sepsis.

Postoperative Morbidity

Complications seen after THE were temporary recurrent nerve injury in 5 patients and permanent recurrent nerve injury in 2 patients for a total incidence of 9%. There were two recurrent nerve injuries in the TTE group. Nonlethal respiratory difficulties occurred in both groups. This was severe enough to require a tracheostomy in 2 patients after TTE and 2 after THE. One episode of chylothorax occurred after THE. As mentioned previously there were two fatal tracheal injuries in the THE group, both occurring in patients with laryngocervical malignancies that had undergone preoperative radiotherapy. An additional patient with a tumor located in the proximal thoracic esophagus suffered an intraoperative tracheal laceration during THE. This patient also had received preoperative radiotherapy. The injury was recognized and repaired intraoperatively and the patient was discharged 10 days after operation. The fact that all three tracheal injuries in our series occurred in patients who had preoperative radiation therapy to lesions in the proximal esophagus suggests the membranous portion of the trachea is particularly vulnerable to dissection injury under the circumstances. Extreme care should be taken to perform the proximal dissection of the trachea from the esophagus under as much direct view as possible in an irradiated field. The THE and TTE groups each had one major

Table 2. Morbidity and Mortality of Transhiatal Esophagectomy Related to Site of Malignancy[a]

Variable	Site: Laryngocervical	Site: Upper Thoracic	Site: Lower Thoracic	p Value
No. of Operations	24	16	30	
Intraoperative blood loss (mL)	1,190 ± 245	630 ± 175	525 ± 140	<0.05[b]
Operative time (h)	6.3 ± 0.6	4.6 ± 0.4	5.2 ± 0.4	<0.05[b] <0.07[c]
Postoperative hospital stay (days)	22.0 ± 3.1	15.8 ± 2.7	25.4 ± 7.4	NS
Operative deaths	4	1	1	

[a] Where applicable values are shown as mean ± standard error of the mean. [b] Lower thoracic versus laryngocervical. [c] Upper thoracic versus laryngocervical.

NS = not significant.

anastomotic leak that resulted in clinical sepsis and delayed resumption of oral intake more than 1 week. There were 18 minor anastomotic leaks in the THE group and 1 minor leak in the TTE group. An anastomotic leak was defined as any leak on the barium swallow that was performed routinely from 5 to 7 days after operation on all patients. Nine of these 19 leaks were clinically asymptomatic.

Analysis of operative and postoperative characteristics for THE performed for malignancies at different levels was performed (Table 2). Laryngocervical lesions were associated with a significantly greater blood loss and operative time than intrathoracic malignancies. Twenty of the 24 laryngocervical lesions were joint operations with the Head and Neck Service. Resection of the primary malignancy before THE and gastric interposition may explain the additional operative time and blood loss. There was no significant difference in operative time or blood loss between THE done for upper and for lower thoracic malignancies.

The total number of THE and TTE procedures was recorded for each year of this study (Fig 1). There was no protocol throughout the study among the operating surgeons designating which procedure to do. The absolute number of TTEs remained relatively steady, but the absolute number of THEs increased as more patients were considered to have operable disease. In addition, as experience with THE accumulated the procedure began to be done for benign esophageal diseases. Transhiatal esophagectomy for benign conditions accounted for 20% of the total number of esophagectomies in the last half-year of the study. Benign conditions treated with THE were severe recurrent reflux strictures (2 patients), end-stage achalasia with stricture (1), previous hiatal hernia operation with stricture (2), and acute instrumental perforation (2). There were no postoperative deaths and no intraoperative bleeding problems or tracheal injuries in the group with benign disease. Morbidity was confined to one temporary recurrent laryngeal nerve injury and two anastomotic leaks that progressed to strictures after the patients left the hospital. The strictures were managed successfully with outpatient balloon dilation.

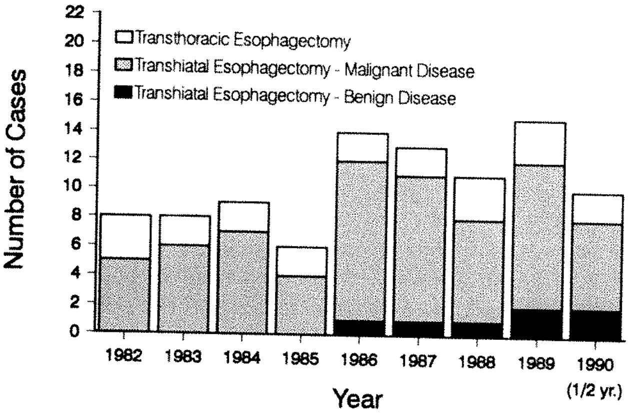


Fig 1. Esophagectomies performed yearly from 1982 to 1990, with bar graphs showing the number that were transthoracic, transhiatal for malignancy, and transhiatal for benign disease.

Comment

Perhaps the greatest concern over the use of THE has centered over the lack of direct visualization of the dissection of the upper thoracic esophagus with the risk of increased blood loss and potential catastrophic bleeding. Fok and colleagues [3] reported an 18% incidence of bleeding severe enough to cause hypotension while performing THE. Orringer [6], however, described no intraoperative bleeding severe enough to require a thoracotomy or sternotomy for control in his first 100 cases. In our study the mean blood loss using both operations was relatively small and of equal degree. However, we did experience two episodes early in our experience with THE in which massive bleeding occurred (3% incidence). One of these episodes contributed to a postoperative death. We suspect our incidence was less than that reported by Fok and colleagues because we preferred to use TTE for bulky proximal thoracic esophageal lesions. This selection criterion has also been described by Murray [7] and Terz and associates [8].

Our study showed the length of operation to be almost 2 hours less when THE was used rather than TTE. Hankins and co-workers [5] reported the same finding, but also observed—as we did in our present study—that this shorter operative time did not translate into a lower morbidity or shorter average postoperative stay. We saw a bimodal postoperative pattern characterized by a very smooth recovery for the majority of patients after THE with 52% discharged by 2 weeks and 71% discharged by 3 weeks. However, complications occurring in one-third of the patients brought the average length of stay after operation out to a level seen with TTE. Orringer [6] reported 80% of his patients being discharged after THE by the end of the third week, which is similar to our results.

Transhiatal esophagectomy in our study was associated with a significantly increased number of anastomotic leaks compared with TTE. Others have reported similar findings [5, 6]. Our experience, like theirs, showed these cervical leaks to be easily managed with no mortality. Balloon dilation appeared to speed the closure of these fistulas [9, 10].

Four of the six deaths seen after THE were associated with operations for laryngocervical malignancies where THE was used to supply a gastric tube for interposition. Operations for malignancies at this level in our series clearly had the highest morbidity and mortality rate (17%). Ujiki and colleagues [11] reported a comparable mortality rate of 19% for THE used to replace the pharyngoesophagus. If one compared THE to TTE performed only for intrathoracic lesions the mortality rate for THE in our series was only 4%, whereas that for TTE was 8%.

Our study showed that THE was a faster operation than TTE and was not associated with an increased mean blood loss. Although more than two-thirds of our patients were discharged within 3 weeks of operation after THE, serious complications did occur. The absence of a thoracic incision did not prevent serious postoperative pulmonary complications in the THE patients. Operations for malignancies at the laryngocervical level combined with THE and gastric interposition had substantial morbidity and mortality, whereas THE performed for benign lesions had no mortality and a low morbidity. Transthoracic esophagectomy remains our choice for bulky proximal thoracic malignancies. Transhiatal esophagectomy remains our choice for early intrathoracic esophageal malignancies at any level, for bulky distal esophageal lesions, and for benign conditions requiring total esophagectomy.

References

1. Orringer MB, Sloan H. Esophagectomy without thoracotomy. J Thorac Cardiovasc Surg 1978;76:643–54.
2. Barbier PA, Becker CD, Wagner HE. Esophageal carcinoma: patient selection for transhiatal esophagectomy. A prospective analysis of 50 consecutive cases. World J Surg 1988;12:263–9.
3. Fok M, Siu KF, Wong J. A comparison of transhiatal and transthoracic resection for carcinoma of the thoracic esophagus. Am J Surg 1989;158:414–8.
4. Goldfaden D, Orringer MB, Appelman HD, Kalish R. Adenocarcinoma of the distal esophagus and gastric cardiac. Comparison of results of transhiatal esophagectomy and thoracoabdominal esophagogastrectomy. J Thorac Cardiovasc Surg 1986;91:242–7.
5. Hankins JR, Attar S, Coughlin TR Jr, et al. Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg 1989;47:700–5.
6. Orringer MB. Transhiatal esophagectomy without thoracotomy for carcinoma of the thoracic esophagus. Ann Surg 1984;200:282–8.
7. Murray GF. Esophagectomy without thoracotomy [Editorial]. Ann Thorac Surg 1986;41:233–4.
8. Terz JJ, Beatty JD, Kokal WA, Wagman LD. Transhiatal esophagectomy. Am J Surg 1987;154:42–8.
9. Delange EE, Shaffer HA Jr, Daniel TM, Kron IL. Esophageal anastomotic leaks: preliminary results of treatment with balloon dilation. Radiology 1987;165:45–7.
10. Orringer MB, Lemmer JH. Early dilation in the treatment of esophageal disruption. Ann Thorac Surg 1986;42:536–9.
11. Ujiki GT, Pearl GJ, Poticha S, Sisson GA Sr, Shields TW. Mortality and morbidity of gastric "pull-up" for replacement of the pharyngoesophagus. Arch Surg 1987;122:644–7.

DISCUSSION

DR EDDIE L. HOOVER (Buffalo, NY): I enjoyed the presentation very much, and I too have been intrigued by this approach. My question is related to patient selection. Every time I do this operation through the classic Ivor-Lewis approach, I am always shaving tumor off of something. I just do not see the patient at an early stage where I can jiggle the esophagus loose through a transhiatal approach. How do you make that determination as to whether or not you can safely do that, with this disease being so hard to define in terms of true surgical staging despite the use of a computed tomographic scan? We have not found magnetic resonance imaging to be very useful in assessing the extent of mediastinal adenopathy and adherence to the aorta and other structures. Have you ever had to abandon the closed approach and revert to an open procedure? If so, are you able to predict which patients are not candidates for the transhiatal approach?

DR DANIEL: If we think by computed tomographic scan that we are going to have a tumor abutting the trachea or the aorta, we will skip the neck incision, do the abdominal part, and begin our blunt dissection; if we see it is too close for us to think we can safely do it, then we proceed with an Ivor-Lewis procedure.

The other whole issue, though, remains to be sorted out, and that is, is this a good cancer operation? We did not attempt to answer that with this study.

DR HARVEY I. PASS (Bethesda, MD): In your patients, exclusive of the laryngocervical group, have you looked back at the values of forced expiratory volume in 1 second and forced vital capacity and tried to match them and see whether you have comparable groups? Only then could you look at those comparable groups for specific complications comparing one operation with the other and then analyze whether you have had any difference in pulmonary complications. Could it be that one group indeed was selected for transhiatal esophagectomy because they had poor pulmonary function to begin with?

DR DANIEL: We have not. We have been very impressed with how thoracotomy patients have responded to thoracic epidural anesthesia, and that might shift the equation back to what might be a better cancer operation if the statistics suggest that it is better.

DR KAMAL A. MANSOUR (Atlanta, GA): I have a couple of questions. First, is the operative time that essential? Does the difference of 2 hours make you change your approach from transthoracic to transhiatal? Or is it something more important than that? What about patient's safety? And your nerves?

Regarding the second question, you said the groups are equal in morbidity. I notice that you have two massive aortic hemorrhages, you have 18 leaks, you have seven episodes of recurrent laryngeal nerve paralysis—I do not think these are comparable. I think we need to really reassess our intentions in doing esophageal surgery rather than the length of the surgical procedure. If it is easier on the patient, that is different, and that is the question. You had 2 patients who had poor pulmonary functions and you did a thoracotomy. Maybe these patients are the ones in whom you should do a transhiatal rather than transthoracic esophagectomy. And the second point is, you had 18 cervical leaks. Did you have a higher incidence of postoperative strictures due to the leaks?

DR DANIEL: I thank you, Dr Mansour, for your questions. I do not care how good you are, how small your hands are, there are going to be a few patients who are going to hemorrhage or have a serious complication related to blunt dissection. One reason we did this study was try to quantitate what we thought was a better operation. We were surprised we could not prove statistically that patients got home quicker after transhiatal procedures.

As far as your question about the leaks and strictures, yes, most of the time when we did have a serious leak it was followed later on, within several weeks, by a stricture. This has been easily managed in our institution by outpatient dilation.

DR THOMAS W. RICE (Cleveland, OH): I wonder about your experience with transhiatal esophagectomy for benign disease. The esophagus is end-stage and has been probably been operated on before. Do you have any comments on the mobilization of the esophagus in the previously operated field? Can you comment on the cardia, which has been used for a previous fundoplication? Have you ever been trapped with not enough gastric length to reach into the neck with a transhiatal esophagectomy for benign disease?

DR DANIEL: Yes, 1 patient had a previous Nissen operation and the stomach pedicle would not reach the neck. Previous left thoracotomies do not prohibit a transhiatal operation. We were able to do sharp dissection and separate the lung and other adhesions from the esophagus in 2 patients who had had previous left thoracotomies for esophageal hernia repair.

The Learning Curve for Intraoperative Echocardiography During Congenital Heart Surgery

Ross M. Ungerleider, MD, William J. Greeley, MD, Ronald J. Kanter, MD, and Joseph A. Kisslo, MD

Department of Surgery, Duke University Medical Center, Durham, North Carolina

Our group has previously reported a large prospective experience with the use of intraoperative echocardiography with Doppler color-flow imaging (IE-DCFI) during the repair of congenital heart defects. We have now performed IE-DCFI in 621 patients and have observed a major change in the impact of this technology, which has stabilized during our most recent experience (the last 207 patients). To evaluate the surgical learning curve with IE-DCFI, we divided patients into three groups: group 1, patients 1 through 207; group 2, patients 208 through 414; and group 3, patients 415 through 621. There were no major differences between groups with respect to age or disease entities. The average time needed to perform an IE-DCFI examination decreased from 3.75 ± 1.77 minutes in group 1 to 3.35 ± 1.52 minutes in group 2 and has remained stable. The number of patients requiring revisions in the operating room (based on IE-DCFI findings) decreased from 17 (8%) in group 1 to 7 (3%) in group 2 to 5 (2%) in group 3. Furthermore, revisions were 100% successful in correcting the problem in groups 2 and 3, whereas 18% of group 1 patients left the operating room with persistent residual defects by IE-DCFI. Surgeons can acquire the ability to interpret the results of IE-DCFI themselves and use it to enhance their operative repair of congenital heart defects, but this requires an experience of at least 200 cases. Once skills are refined, the technique will identify 2% to 3% of patients who would benefit from operative revision before leaving the operating room and will direct that revision. As we learned to more accurately evaluate IE-DCFI data, the likelihood of a good outcome for patients leaving the operating room without IE-DCFI-identified problems improved from 88% in group 1 to 95% in group 2 to 97% in group 3.

(Ann Thorac Surg 1992;54:691–8)

Intraoperative echocardiography is becoming an increasingly used technology for the evaluation of repair of congenital heart defects, but familiarity with its use by surgeons remains the single most important limitation to its application in any given institution. Although pediatric cardiologists and anesthesiologists are helpful in obtaining and interpreting echocardiographic images, it is the surgeon who has the most cogent understanding of the anatomy and the most lucid mental image of the complex intracardiac spatial relationships created by the reconstruction. Only the surgeon can relate ultrasound images to his or her own personal concerns with respect to specific areas of the repair. In this sense, it is the surgeon who should be most capable of interpreting the intraoperative echo in relation to his or her knowledge of how the repair proceeded and attach appropriate relevance to the echo findings.

Nevertheless, surgeons are not ordinarily trained in echocardiography, and the advantages that surgeons possess for performing clinically relevant and precise interpretation of intraoperative echocardiograms is more often than not neutralized by lack of experience with and understanding of this technology. However, with assistance from cardiologists and anesthesiologists, a congenital heart surgeon can learn how to obtain and interpret his or her own images and make decisions regarding the quality of repair that will enhance the patient's long-term outcome. Although the refinement of these skills probably occurs over the course of a career, this report describes the learning curve that should be expected and accepted by a surgeon who wishes to eventually become competent with this technology.

Material and Methods

Intraoperative echocardiograms were obtained before and after repair from 621 patients undergoing repair of congenital heart defects on cardiopulmonary bypass through a median sternotomy. The majority of these examinations were performed using an epicardial technique previously described by our group [1]. In some patients, transesophageal echocardiography was also performed depending on the nature of the defect. A cardiology colleague scrubbed and assisted with the epicardial imaging during the first 300 cases. Nevertheless, the surgeon attempted to obtain views in all patients, and ultimately (the last half of the series) a cardiologist scrubbed to assist the surgeon in obtaining images only if specifically requested to help evaluate a particular problem. All images were recorded on high-fidelity tape and were later reviewed by cardiologists experienced in echocardiography. However, decisions made at the time of operation were based on

---

Presented at the Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, FL, Nov 7–9, 1991.

Address reprint requests to Dr Ungerleider, Department of Surgery, Duke University Medical Center, Box 3178, Durham, NC 27710.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Outcome Relating to Final Echo Results[a]

Postrepair Grade	No. of Patients[b]	Reoperation
Echo perfect	375 (60)	2 (0.5)
Acceptable residual	204 (33)	20 (10)
Unacceptable residual	39 (6)	13 (33)

[a] Numbers in parentheses are percentages. [b] Percentages are based on entire series of 621 patients.

real-time information and on the operating team's impression of these data.

Although the results of prospective information generated from the first half of the patients in this study have been previously reported, this particular study analyzes the data from 621 patients in a retrospective fashion to identify (1) the incidence of repair revision in the operating room based on information generated by echocardiography performed after bypass and (2) the ability of the surgeon to properly identify an acceptable repair (by evaluating the need for reoperation for patients over the entire course of the study). Patients were divided into three groups based on chronological appearance in the series. Patients were entered if they met the criteria of undergoing correction of a congenital cardiac defect through a median sternotomy on cardiopulmonary bypass. The first entry (patient 1) was in March 1987 and the final entry, July 1991. For the purposes of retrospective analysis, patients 1 through 207 were labeled as group 1 (the early experience), patients 208 through 414 as group 2 (the intermediate experience), and patients 415 through 621 as group 3 (the most recent experience). Patients ranged in age from 1 day to 59 years, with 240 patients (39%) less than 1 year of age and 417 (67%) less than 3 years of age. The smallest patient in the series weighed 1,700 g and underwent closure of a ventricular septal defect.

Patients were followed up with respect to outcome after operation. A bad outcome was considered to be reoperation (for a residual defect) or death. Reoperation that occurs as the natural history of an operative procedure (eg, conduit replacement after a Rastelli procedure) was not coded as a bad outcome, but the need for valve replacement after valve repair was considered an operative failure, and the reoperation was coded as such. Follow-up has been complete as of November 1, 1991. This allows a full 3 months of follow-up since the latest entry in the series. It has been our experience through the evolution of this series that the majority of infants who require reoperation for failure of a previous procedure do so within the first 6 to 8 weeks after operation.

Table 2. Outcome Relating to Final Echo Results[a]

Postrepair Grade	Group	No. of Patients[b]	Reoperation
Echo-perfect	1	138 (67)	2 (1.4)
	2	124 (60)	0
	3	113 (55)	0
Acceptable residual	1	47 (23)	13 (28)
	2	68 (33)	4 (6)
	3	89 (43)	3 (3)
Unacceptable residual	1	20 (10)	8 (40)
	2	14 (7)	4 (29)
	3	5 (2)	1 (20)

[a] Numbers in parentheses are percentages. [b] Percentages are based on number of patients in each group.

Results

All three groups were equivalent with respect to major cardiac defects, male to female ratio, and age distribution. With experience, it was found that the average time for an intraoperative epicardial echo examination fell from 3.75 ± 1.77 minutes in group 1 to 3.35 ± 1.51 minutes in group 2 and has remained relatively stable over the recent months. The time for an examination is initially dependent on surgeon familiarity and skill with the technique but eventually is related more to the nature of the cardiac defect, the information needed, and the echogenicity of the patient.

Results were graded as follows: (1) "echo-perfect" (no discernible residual defect, with good ventricular function and a repair that met or exceeded all expectations); (2) "acceptable" residual defect (a repair that disclosed discernible residual defects that were not thought to be major and that could be consistent with a good outcome); or (3) "unacceptable" residual defect (signifying a suboptimal result; often these patients were not considered to be in a condition that allowed revision of the repair, or it was not thought that the repair could be performed any better). Table 1 shows the correlation of final echo results as they were coded at the completion of each procedure with the incidence of reoperation during follow-up. Table 2 separates these results by patient groups. It is notable (Table 2) that with increasing experience and skill (groups 2 and 3) in obtaining intraoperative images, surgeons are more likely to find residual defects and are less likely to code the repair as echo-perfect. Nevertheless, the understanding of which results truly are acceptable correlates with increasing experience, and the incidence of patients requiring reoperation in this category becomes a very appropriate 3% to 6%. Furthermore, with improved skills (as echo teaches the surgeon how and where to avoid technical errors), the incidence of an unacceptable technical result becomes less common.

During the course of the study, records were maintained on all patients who had revision of the repair in the operating room based on echo information alone. In the initial phases of the study, oxygen saturation information or green dye curves were obtained to verify the importance of the echo findings. However, the correlation was not always accurate, and it was found that with improved understanding of the echocardiographic images, the surgeons were able to obtain a much more sensitive impression of the repair quality as well as specific information regarding any regions of difficulty [2]. Table 3 lists the number of revisions performed in each group on patients whose repairs were suboptimal and notes whether or not the revision was successful in producing a good operative result. Intraoperative revision was "common" in group 1 and was not always successful in producing a good technical result. With experience, it was found that the need of revision of the operation decreased but was still necessary in 2% to 3% of patients (groups 2 and 3). In these latter groups, echo invariably guided the surgeon efficiently and in a specific manner to achieve a technically good result.

The surgeon's impression of the postrepair echo results and the patient's long-term outcome were compared. Death or the need for reoperation during follow-up was considered a bad outcome. Any concern with the postrepair echo was noted, including residual defects, severe ventricular dysfunction, or serious remaining abnormality of the reconstructed anatomy. Patients for whom there were no concerns regarding the postrepair echo (473 patients, 76%) had an excellent likelihood (92%, 434 patients) of a good long-term outcome, but this likelihood fell to 41% (61 patients) for patients whose postrepair echo demonstrated *any* reason for concern (24%, 148 patients).

Table 4 reexamines these data with respect to the study groups and demonstrates that with experience (groups 2 and 3), the ability of the surgeon to correlate the postrepair echo with the likelihood of a good long-term outcome approaches 95% to 97%. Likewise, based on our current experience, the likelihood of a good outcome when there is a reason for concern regarding the postrepair echo falls to only 24%.

Comment

Intraoperative echocardiography has been reported by us [2, 3] and several others [4–9] to be beneficial during the repair of congenital heart defects. The purpose of this report is not to revalidate this concept, although this conclusion could again be clearly drawn from the substantial documentation that has accumulated from this large series of 621 patients. Rather, it has been our interest to display these data in a retrospective fashion to demonstrate what became intuitively obvious to us throughout the course of the study—that there is a synergistic relationship between a surgeon's experience and the contributions of intraoperative echocardiography.

A learning curve is a subjective impression acquired by a surgeon that he or she has gained important experience dealing with a set of problems and that this has contributed to an improvement in results during the involved time frame. There has been a clear improvement in surgical results within the time frame of this study. We have not reoperated on a single patient for residual ventricular septal defect since 1988, and we are thoroughly and enthusiastically convinced that information obtained from intraoperative echocardiography has resulted in the more rapid evolution of proper surgical techniques with immediate reinforcement of the most effective methods for repairing a variety of defects.

The fact that a surgical team can learn to use intraoperative echocardiography to make relevant and appropriate decisions is underscored by the fact that a cardiologist was not routinely present during the operations on the last 300 patients in this series. It was during this same period that the most dependable correlation was being obtained between the intraoperative echo and the ability to associate the findings with patient outcome.

For a surgical team to acquire the necessary skills and experience with this technology, it is important for them to have adequate and committed support and supervision during the early phases of learning. In our case, we were fortunate to have the consistent and dedicated involvement of an experienced echocardiographer (J.A.K.) for *every* procedure performed in group 1 and many of the procedures in group 2. Surgeons can be taught how to manipulate an epicardial transducer and to interrogate intracardiac anatomy in a thorough and accurate fashion. The process of placing a transducer on the heart is not difficult, but the ability to interpret the images generated and the manipulation of the probe to display unusual but important views [10, 11] are acquired skills that must be taught and learned over time.

Comparison of Tables 1 and 2 demonstrates the impact of experience. When evaluated as a complete series of 621 patients, it appears that leaving the operating room with an acceptable residual defect, as demonstrated by postrepair echocardiography, is a risk factor for reoperation. If this were truly the case, then selection of the term *acceptable* for these residual defects would be inappropriate. However, reevaluation of our evolution of the term *acceptable*, when analyzed by looking at the early versus the later patients in the series, demonstrates that with experience, the surgical team is able to learn how to better correlate an acceptable residual defect with the reality of long-term outcome. It is interesting that as experience with the technology increased, it was less likely for us to find an echo-perfect repair despite the fact that the nature

Table 3. Revisions in Operating Room for 621 Patients[a]

Patient Group	Revisions Based on Echo	Good Result
1	17 (8)	14 (82)
2	7 (3)	7 (100)
3	5 (2)	5 (100)

[a] Numbers in parentheses are percentages.

Table 4. Outcome Relating to Echo Results[a]

Postrepair Echo Results	Group	No. of Patients[b]	Good Outcome
No concerns	1	140 (68)	115 (82)
	2	155 (75)	147 (95)
	3	178 (86)	172 (97)
Reason for concern	1	67 (32)	37 (55)
	2	52 (25)	17 (33)
	3	29 (14)	7 (24)

[a] Numbers in parentheses are percentages. [b] Percentages are based on number of patients in each group (n = 207).

of operations between groups was essentially the same. It is also interesting that there were two reoperations in group 1 for patients who presumably left the operating room with an echo-perfect repair. More likely, with increased skill in using this technology, the surgical team became better capable of recognizing, and recording as such, echo-imperfect repairs for reasons that might have been unappreciated in the early part of the series.

Correlating with this is the increase in acceptable residual defects in group 3 compared with group 1. Again, this is probably a reflection of more experience in interpretation of the postrepair echo. Most importantly, however, there was a better understanding of what truly constituted an acceptable residual defect by the time our series had reached 200 patients so that the incidence of reoperation in this group of patients became more consistent with the term *acceptable*. Although the definition of acceptable is relatively subjective, it is important to emphasize the fact that with time and experience, a surgeon who pays attention to how the postrepair echo findings compare with patient outcome will eventually be able to have an increasingly clear understanding of what constitutes an acceptable residual defect after the repairs. A learning curve comprises subjective interpretation of experience. In the case of intraoperative echo, learning results in (1) better recognition of small residual defects, (2) more accurate prediction of which defects by echo are acceptable (as supported by correlation with acceptable outcome for the patient), and (3) fewer unacceptable results (by echo), probably because of improved surgical technique.

In the early part of the series, it was not uncommon to revise an operation before the patient was taken from the operating room. The 8% incidence of intraoperative revision based on echo findings in group 1 was considered somewhat high (see Table 3). However, with improved understanding of problem areas with certain repairs, results improved quickly, and by the time we had reached 200 patients, the need to revise repairs had decreased substantially and has remained relatively stable at 2% to 3%. During this time, we [12] have evolved improvements on repairs of some defects based on echo findings. Although oxygen saturations and green dye curves were obtained early in the series in an effort to determine the sensitivity of the intraoperative echo, it was quickly learned that these less specific methods were less reliable and had no capacity to demonstrate to the surgeon the specific region of difficulty [2]. Instead we have learned to evaluate the importance of residual defects using a number of criteria that correlate well with outcome. For example, residual ventricular septal defects are thought to be important if (1) the defect can be seen by two-dimensional imaging without color flow, (2) substantial turbulence can be seen on both sides of the defect, (3) the amount of turbulence in the right ventricle is substantial and fills a large part of the chamber as opposed to presenting as a small or well-defined jet, (4) turbulence is noted in an area where the surgeon was concerned with the technical repair, or (5) marked turbulence is noted by color-flow mapping in a common trouble spot (Fig 1).

The most immediate useful function of postrepair echo is to help identify those patients who will benefit from revision before they are taken from the operating room. Although it can be claimed that the reduction in the need for this intervention as the series progressed is due to more surgical experience and better surgical skills, we are confident that the synergistic impact that echocardiography has on the evolution of good surgical techniques is enhanced by a surgical team willing to learn this technology so that the learning curves of surgical technique and ability to evaluate echo complement one another. Furthermore, because the system becomes so easy to use (with a little practice) and because it can be potentially useful in any patient, we currently recommend routine use after repair. In a properly equipped operating room, routine evaluation takes less time and can be more helpful than trying to decide which patients should have imaging depending on results of other screening techniques (eg, oxygen saturations and dye curves). As the typical echo takes 2 to 3 minutes, a surgeon can know quickly and with great confidence that the ventricular septal defect is well closed or that a repaired valve is functioning well.

In the process of learning techniques to evaluate the presence of residual defects, we found several technical considerations useful: (1) It is important that the transducer make good contact with the epicardial surface. Although this may induce some ectopy, the ectopy is usually well tolerated by the patient and rarely results in hemodynamic compromise. (2) Patients vary with respect to their echogenicity, and occasionally there are patients in whom echo evaluation is more difficult. It is in these patients that experience is useful in enabling the surgical team to interpret information that is less than optimal in quality. Early during a team's experience, these poor-quality examinations must be tolerated, and in time, the information they provide will become more apparent. (3) The use of transesophageal echocardiography in conjunction with epicardial echocardiography is quite helpful. Prosthetic patch material often causes interference with sound wave transmission below the patch, making it difficult to evaluate certain areas after repair [6]. The use of the epicardial and transesophageal approaches concurrently reduces error in interpretation resulting from patch dropout. (4) It is helpful to interrogate the repair briefly during the period of rewarming. This can be done, once the heart has resumed an appropriate rhythm, by temporarily reducing venous return to the pump and by ventilating the lungs. This restores a more normal physiology and enables interrogation of the repair quality. In the occasional instance when an unexpected problem is found with the repair (such as a residual ventricular defect), revision can be performed in an efficient and timely manner without having waited for rewarming and weaning from bypass. Nevertheless, it is important to repeat the examination after the patient has been weaned from bypass. This is especially critical when evaluation requires the more normal loading conditions that exist off cardiopulmonary bypass (such as evaluation of mitral valve function).

Recent enthusiasm [13, 14] for the application of newer transesophageal technology to the infant patient after

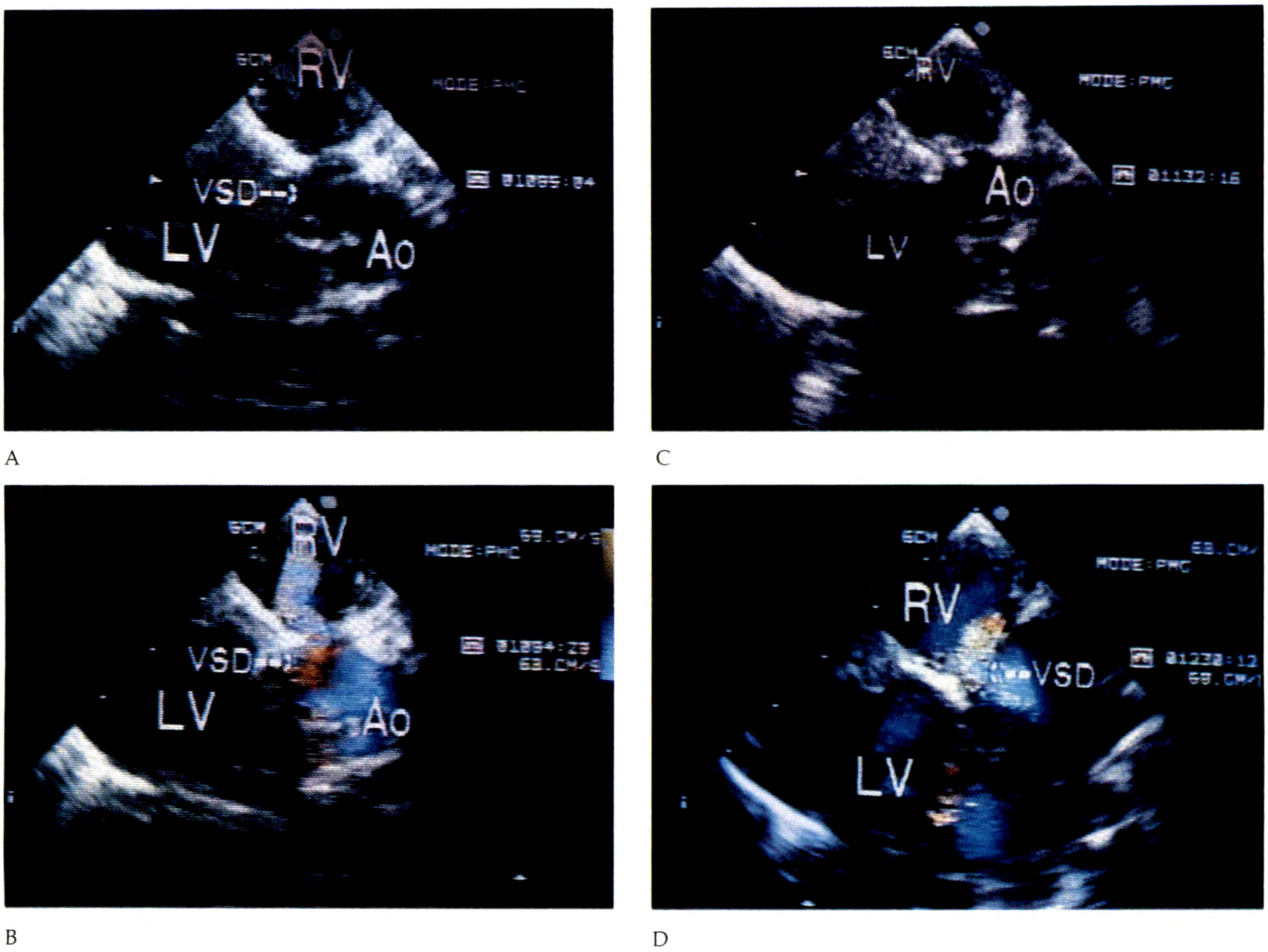


Fig 1. (A) Long-axis view of a residual ventricular septal defect (VSD) *after repair of an atrioventricular canal defect. The* broken white arrow *demonstrates the location where turbulence will begin when color flow is added. The* black arrow *demonstrates a discernible residual defect that can be appreciated as a gap between the patch and the aortic annulus and that can be visualized without the addition of color flow. (B) Turbulence begins below the patch and extends through the defect to fill the right ventricular cavity. (C) Repair of this area. The pledgets used for the suture repair of this defect can be appreciated, and the defect can no longer be visualized without color flow. (D) Although there is still a remaining residual defect, it is quite acceptable. Turbulence does not extend very far into the right ventricular cavity, and there is no major turbulence below the patch.* (Ao = *aorta;* LV = *left ventricle;* RV = *right ventricle.)*

surgical repair deserves comment. Although transesophageal echocardiography is a useful and effective method, the relative nonparticipation by the surgeon may inhibit full concentration by the surgical team on learning to appreciate echocardiographic images. The epicardial approach gets the surgeon involved and enables him or her to interrogate the quality of the repair with the spatial knowledge of that repair that *only* the surgeon has. This is not to say that transesophageal echocardiography will not be helpful. It is extremely useful for certain problems (eg, mitral valve function below a prosthetic patch or continuous assessment of ventricular function). However, in the hands of an experienced surgical team, the value and efficacy of epicardial echo in allowing the surgeon to quickly validate the quality of the technical repair should not be minimized. Even as better technology provides biplane transesophageal echocardiographic probes in infant sizes with reasonable resolution, the same advances will propel corresponding improvements in the epicardial transducers, and once surgeons learn to use the epicardial approach, the transducers become "omniplane."

With experience comes an appreciation for those problems disclosed by the postrepair echo that correlate with a bad outcome (ie, death or the need of reoperation). The more recent groups in our series demonstrated excellent correlation of prognosis and postrepair echo findings, suggesting that after approximately 200 intraoperative echo examinations, a surgical team is able to very reliably predict which patients have the highest likelihood of a good outcome based on the postrepair echo findings. Although the terms used to categorize the repairs seem subjective, long-term outcome is objective, and once outcome correlates with the subjective appreciation of the surgical repair (by echo), then the team will know that it has learned to accurately understand the intraoperative information.

The most difficult portion of the learning process for the surgical team is to react appropriately to a disturbing postrepair echo finding. It is easy for the team to become overly zealous and attempt to achieve echo-perfect results with each repair. This is clearly unnecessary and not always in the patient's best interest. Conversely, it is sometimes emotionally difficult for a surgeon to demonstrate a technically less than perfect repair to all members of the operating team and remain feeling secure that the result is truly acceptable. Most agonizing of all are those circumstances where an unexpected but major residual problem is disclosed that requires repeat surgical intervention. These patients frequently have no concomitant clinical problems and can easily be weaned from bypass. The problem can be ignored and the patient can be returned to the intensive care unit in good condition. The agonizing part is that the surgical team learns with time that these patients "will be back," and it becomes far easier to do something sooner rather than later [11]. With acquired skill in interpreting the intraoperative echo, the surgical team will find that the surgical procedures will less frequently repeat problems of previous cases.

In conclusion, dedicated use of intraoperative echocardiography during the repair of congenital heart defects in 621 patients by the same surgical team demonstrates four important points. (1) Intraoperative echocardiography can be learned by the surgical team to provide information that can prevent patients from leaving the operating room with a suboptimal repair. (2) The surgical learning curve for this technique is approximately 200 cases, but refinements in the ability to use this information continue beyond 600 cases. (3) With experience, postrepair echo can be expected to provide information that will encourage revision of the repair before the patient leaves the operating room in 2% to 3% of cases. The specific information provided by echo enables these revisions to have a high degree of efficiency and success. (4) Once skills are mastered, the ability to correlate intraoperative echo with outcome approaches 97%.

We thank James NeSmith (RDCS) for his technical assistance in the preparation of the manuscript.

References

1. Ungerleider RM. The use of intraoperative echocardiography with Doppler color flow imaging in the repair of congenital heart defects. Echocardiography 1990;7:289–304.
2. Ungerleider RM, Greeley WJ, Sheikh KH, Kern FH, Kisslo JA, Sabiston DC Jr. The use of intraoperative echo with Doppler color flow imaging to predict outcome after repair of congenital cardiac defects. Ann Surg 1989;210:526–34.
3. Ungerleider RM, Kisslo JA, Greeley WJ, Van Trigt P, Sabiston DC Jr. Intraoperative prebypass and postbypass epicardial color flow imaging in the repair of atrioventricular septal defects. J Thorac Cardiovasc Surg 1989;98:90–100.
4. Canter CE, Sekarski DC, Martin TC, Guitierrez FR, Spray TL. Intraoperative evaluation of atrioventricular septal defect repair by color flow mapping echocardiography. Ann Thorac Surg 1989;48:544–50.
5. Gussenhoven EJ, van-Herwerden LA, Roelandt J, Ligtvoet KM, Bos E, Witsenburg M. Intraoperative two-dimensional echocardiography in congenital heart disease. J Am Coll Cardiol 1987;9:565–72.
6. Hagler DJ, Tajik AJ, Seward JB, Schaff HV, Danielson GK, Puga FJ. Intraoperative two-dimensional Doppler echocardiography. A preliminary study for congenital heart disease. J Thorac Cardiovasc Surg 1988;95:516–22.
7. Sutherland GR, van-Daele ME, Stumper OF, Hess J, Quaegebeur J. Epicardial and transesophageal echocardiography during surgery for congenital heart disease. Int J Card Imaging 1989;4:37–40.
8. Dan M, Bonato R, Mazzucco A, et al. Value of transesophageal echocardiography during repair of congenital heart defects. Ann Thorac Surg 1990;50:637–43.
9. Hsu YH, Santulli T Jr, Wong AL, Drinkwater D, Laks H, Williams RG. Impact of intraoperative echocardiography on surgical management of congenital heart disease. Am J Cardiol 1991;67:1279–83.
10. Ungerleider RM. In: Karp RS, Laks H, Wechsler A, eds. Epicardial echocardiography during repair of congenital heart defects. Chicago: Mosby-Year Book, 1992:285.
11. Ungerleider RM, Greeley WJ, Sheikh KH, et al. Routine use of intraoperative epicardial echocardiography and Doppler color flow imaging to guide and evaluate repair of congenital heart lesions. A prospective study. J Thorac Cardiovasc Surg 1990;100:297–309.
12. Ungerleider RM. The use of intraoperative epicardial echocardiography with color flow imaging during the repair of complete atrioventricular septal defects. Cardiol Young 1992;2:56–64.
13. Muhiudeen IA, Roberson DA, Silverman NH, Haas GS, Turley K, Cahalan MK. Intraoperative echocardiography for evaluation of congenital heart defects in infants and children. Anesthesiology 1992;76:165–72.
14. Weintraub RG, Sahn DJ. Pediatric transesophageal echocardiography. Present and future. Anesthesiology 1992;76:159–60.

DISCUSSION

DR ROBERT M. SADE (President): This is a very impressive series, particularly with respect to your ability to correlate changes in outcome over time as experience with this technique increased. To what extent do you believe intraoperative echocardiography was actually responsible for improvement in the overall results? How much of the improvement was due to our ability to better manage children postoperatively and to the honing of your personal surgical skills and the skills of the rest of your team? Because many things change over time, in an uncontrolled study like this, it may be difficult to assign alterations in outcome to a particular technical innovation such as the use of echocardiography.

DR UNGERLEIDER: I think you have probably touched on one of the most important features of learning how to use the technology that is available to us, because it is impossible to single out one particular technology that makes all of our changes and improvements possible. I believe it is fair to say that what intraoperative echocardiography is able to do for a surgeon is track that surgeon's progress in learning techniques and probably teach the surgeon how to perform better operations. Some of the results might be due to the improvements in surgical techniques and some, to improvements in learning how to take care of patients postoperatively. Probably there is no clear way to sort out all of these features. What has become clear to us is that if we learn to use the echocardiographic data and if we understand and evaluate these data as objectively as possible, they become a very good predictor for us of how well a patient will do in the postoperative period regardless of all the other factors that might relate to a good outcome.

DR RONALD E. ELKINS (Oklahoma City, OK): That was a very nice presentation. My colleagues and I share your enthusiasm for the use of intraoperative echo. The one area that has plagued us is how to define "acceptable" regurgitation through a repaired mitral valve. Could you give us some insight into what you consider acceptable versus unacceptable in the patient who has undergone atrioventricular canal repair?

DR UNGERLEIDER: Dr Spray, one of the discussants, may be able to answer that question better than I. It has been our impression that almost every patient has some degree of mitral insufficiency discernible by echocardiography after atrioventricular canal repair. In my experience, I have never had to intervene during that particular operation to do anything for that mitral insufficiency. In our series of about 50 patients having atrioventricular canal repair, 2 have had later mitral valve replacement. Neither patient had Down's syndrome, and both left the operating room with very trivial mitral insufficiency.

Assessing mitral insufficiency is difficult; it is probably the hardest assessment to correlate with long-term outcome, but the disease itself helps us appreciate that the condition of some patients will deteriorate in terms of mitral valve function in the long term. Conversely, we have seen some patients with moderate to severe mitral regurgitation after repair of atrioventricular canal who get better postoperatively. Perhaps this is due to the change in systemic afterload when they no longer have such a constricted peripheral circulation.

In summary, we appreciate the degree of mitral insufficiency in the operating room but rarely do anything about it.

DR CONSTANTINE MAVROUDIS (Chicago, IL): This is a very nice report by Dr Ungerleider and his associates and is years ahead of its time. Unlike most operations, which can be visually assessed after completion, intracardiac repairs cannot be seen and must be evaluated by thrills, pressure tracings, oxygen saturation comparisons, and so on. Routine intraoperative echocardiography represents an excellent technique to evaluate intraoperative repairs, which occasionally need to be revised immediately instead of later. It appears that we may have to learn this technique ourselves for a timely evaluation and not depend on our busy cardiology colleagues. Do you foresee extended in-service requirements for the rest of us to acquire these skills? Also, do you think the transesophageal echocardiogram is a little easier to interpret than the epicardial echocardiogram?

DR UNGERLEIDER: Thank you for your kind remarks. To answer first the second question regarding the use of transesophageal technology, that technology is improving. Smaller probes with better resolution will become available. They will be inserted by the anesthesiologist and used to provide continuous on-line monitoring of ventricular function and the repair, and this may make it a little less necessary for surgeons to learn these techniques. However, it has been our impression that epicardial echo adds a lot, especially because in the hands of the surgeon who has performed the repair, it can precisely evaluate areas about which the surgeon has concerns. As you know, there are often instances when you have some concern about an operative repair, and with this technology, you can evaluate it yourself.

With respect to in-service training, learning this technique is much easier than most other aspects of neonatal heart surgery. All it really takes is a surgeon who is willing to tolerate the learning curve of 200 cases, an echo machine in the operating room, and a cardiologist who is willing to help for the first few cases until you learn how to obtain some of the standard views. Then over a few years you will learn how to interpret the information and you will teach yourself. There is really nothing very difficult about this technology.

DR THOMAS L. SPRAY (St. Louis, MO): I compliment Dr Ungerleider for trying to bring this technique to the rest of us who do congenital heart surgery. At St. Louis Children's Hospital, we have been using intraoperative echocardiography with both the epicardial and the transesophageal technique for the past 5 years or so but in more selected patients. I have a comment to make on the issue of mitral regurgitation and then a question to ask.

I think it is difficult to assess the magnitude of mitral regurgitation because it is so dependent on the hemodynamics at the time you are analyzing it. We have found that sometimes jets of mitral regurgitation that look major by echocardiography turn out not to be very important when contrast is added. We inject agitated blood or a mixture of blood and saline solution, which gives a nice microbubble type of contrast and a more quantitative measurement of the magnitude of mitral insufficiency, directly into the left ventricle. On occasion, this technique has allowed us to accept a degree of mitral insufficiency that by regular color Doppler echo we would have thought too severe and we would have repaired. On several occasions in atrioventricular canal repairs, we have had to go back and put in an extra annuloplasty stitch or a stitch in the commissure between the left superior and inferior leaflet components to control what we consider an unacceptable magnitude of mitral regurgitation. So I think echo assessment is very useful after atrioventricular canal repair.

My question is, in how many of your patients with an echo-imperfect result was there a surgical concern at the time? With the large number of patients reported, obviously many did not have an atrioventricular canal or a ventricular septal defect or some kind of intracardiac shunt lesion, but they may have had conduit placement or repair of the right ventricular outflow tract, which we find very difficult to assess echocardiographically by an epicardial technique. In some of these patients, there was minimal concern about your operative repair, and yet echocardiography was used in all of them to see what the repair was like. How many times were you not concerned about your repair and found something on echo that made you want to go back and do something in the operating room?

DR UNGERLEIDER: That question, Dr Spray, is an excellent one. It is humbling for a surgeon to find out that the results in reality are not always the results perceived at the time the repair was finished.

Before we looked at the postrepair echo of the first 328 patients, I was asked by the team, "Well, are you satisfied? Did you do a good job"? And 312 times I said "Yes," and almost 15% of the time, echo disclosed an imperfect repair about which we had some concerns. Whether we did something about it or not, the point is that I was not as happy as I thought I should have been. Sixteen times I told the team, "Gee, that is the best I can do. I am kind of concerned, but I am afraid to try to do more." Thirty percent of the time the repair turned out to be okay. Clearly, an intraoperative assessment based on the surgeon's impression of the results is not always accurate, and echo adds a slightly more objective analysis to the repair evaluation.

And echocardiography continues to affect our results. Just 2 weeks ago we had a visitor, as always happens when this occurs, and I thought we had done an echo-perfect repair of an atrioventricular canal, but when I put the probe on the heart, there was a residual ventricular septal defect in the inlet septum. So a surgeon's impression can sometimes be altered by the echo technology. I think echocardiography continues to add information.

DR ERIC L. CEITHAML (Jacksonville, FL): Dr Ungerleider, I congratulate you on this presentation. My associates and I also use the epicardial echo technique intraoperatively to assess congenital heart repairs, but we have had a difficult time visualizing the right ventricular outflow tract, particularly after homograft reconstruction in patients with tetralogy or pulmonary atresia. Do you use any particular technique to visualize this area?

DR UNGERLEIDER: It is possible to look at the right ventricular outflow tract at least with respect to insufficiency. However, I think it is a misapplication of echo to use it to get an idea of pressure measurements. It is easy for the surgeon to simply insert a needle into various portions of the repair to find out where the pressure gradients, if any, exist. So I think it is wrong to try to make echo something it is not. For right ventricular outflow repair, we recommend pressure measurements.

Emergent Applications of Cardiopulmonary Support: A Multiinstitutional Experience

Jonathan G. Hill, MD, Pamela S. Bruhn, RN, BSN, Sheldon E. Cohen, MD,
Michael W. Gallagher, MD, Frank Manart, MD, Charles A. Moore, MD,
Paul E. Seifert, MD, Paul Askari, CCP, and Candace Banchieri, CCP

Emanuel Hospital and Health Center, Portland, Oregon

The use of emergent portable bypass systems is increasing. Because of limited patient use in any one institution, a combined experience can better determine the applicability of these systems. A total of 187 patients from 17 centers were analyzed. Causes leading to bypass initiation were cardiac arrest (125 patients), cardiogenic shock (44), profound hypothermia (7), pulmonary insufficiency (9), and miscellaneous (2). Weaning from bypass was successful in 30.5% (57 patients). Sixty-four patients (34.2%) were transferred to standard bypass or other modes of circulatory assist. Of the total population, 40 patients (21.4%) were alive greater than 30 days. There were no survivors of unwitnessed arrests. Major diagnostic or therapeutic interventions were carried out on bypass in 74.9% of all patients. In survivors, 77.1% (37/48) had major therapeutic interventions as compared with 50.0% (67/135) of nonsurvivors. Emergency portable bypass systems can successfully resuscitate and support cardiac hemodynamics, although the underlying causes necessitating bypass remain difficult to correct. When corrective intervention can be performed, there is an increased chance of survival. Unwitnessed arrest, prolonged cardiopulmonary resuscitation, and lack of treatment options are relative contraindications. Appropriate patient selection and early application of these systems should lead to improved survival.

(Ann Thorac Surg 1992;54:699–704)

The use of cardiopulmonary bypass for medical emergencies has been advocated since Gibbon [1] proposed the concept for the treatment of pulmonary embolism in 1939. Early trials of emergency bypass systems were initially promising but expediency and technical difficulties prevented their widespread application [2–4]. With the advent of improved femoral cannulas and techniques, emergent bypass applications became more practical [5]. As commercial emergency portable cardiopulmonary bypass systems became more disseminated, the use of these systems has become commonplace.

Single-institutional experiences with commercial and customized emergency systems have been reported [6–10]. These patient sets have been small and reflect widely diverse pathologies. More patients are required to definitively identify those specific causes for which emergent bypass systems are most efficacious. The major challenge is to determine which patients are potentially salvageable, as opposed to those who are either anatomically or metabolically beyond correction and do not warrant further medical intervention. The National Cardiopulmonary Support Registry for Emergency Applications (Appendix 1) was developed to try to meet this challenge. This is the initial report of the Registry.

Material and Methods

Data for patients from 17 institutions were submitted to the National Cardiopulmonary Support Registry. A total of 187 patients were reported from February 1984 to May 1, 1991. Data collection was both retrospective and concurrent. Standard registry forms were submitted, conveying demographics, diagnosis, and procedures (Appendix 2). Definitions of all questions were established before data submission, eliminating as much institutional variability as possible. The tracking of each patient's clinical course during the bypass period was performed, recording the cause of the initiation of bypass, diagnostic and therapeutic interventions, as well as final diagnoses and outcomes (Fig 1). Major events occurring later in the patient's hospitalization were not recorded unless directly related to the bypass period itself. Elective supported angioplasty patients were specifically excluded.

Limited clinical information is usually present at the time of the proposed initiation of emergency bypass. By analyzing clinical variables readily available at a patient's admission, an attempt was made to search for relatively strong early indicators of patient survival. Specific individual variables were analyzed for their ability to assist the physician in deciding if patients should be placed on these systems. The predictive value of each variable was assessed by relative information gain (R) [11]. The R value is a measure of survival/death outcome prediction relative to an infallible predictor. The R value varies from 0 to 1; the closer to 1 the better the prediction.

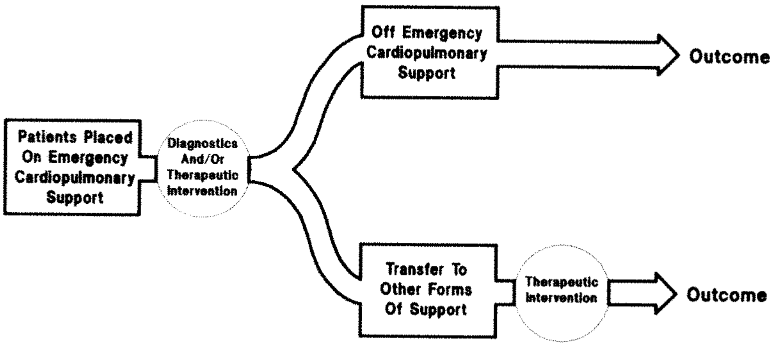
Presented at the Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, FL, Nov 7–9, 1991.

Address reprint requests to the National Cardiopulmonary Support Registry for Emergent Applications, c/o Dr Jonathan G. Hill, 2800 N Vancouver Ave, Suite 242, Portland, OR 97227.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Fig 1. Patient hospital flow: This demonstrates the timing and outcome of major events that occurred during the emergency bypass period. Patients transferred to other forms of support generally had further therapeutic interventions because of the severity of disease.


Patients Placed On Emergency Cardiopulmonary Support
Diagnostics And/Or Therapeutic Intervention
Off Emergency Cardiopulmonary Support
Outcome
Transfer To Other Forms Of Support
Therapeutic Intervention
Outcome

Results

Age/Sex

Emergency bypass was performed on 138 male and 49 female patients. The ages ranged from 2 to 83 years, with an average age of 50.6 ± 17.6 years (± standard deviation).

Cause of Bypass Initiation

Seven major reasons for initiating emergent bypass were categorized: cardiac arrest, 111 patients; cardiac arrest after cardiotomy, 14; cardiogenic shock, 38; cardiogenic shock after cardiotomy, 6; hypothermia, 7; pulmonary insufficiency, 9; and other, 2. In addition, although some patients had arrested, they had not been categorized to an "arrest" cause in considering their initiating diagnosis. Thus, the total number of arrested patients and their initiating diagnosis were also listed (Table 1). Fourteen of the 130 cardiac arrests were unwitnessed. In witnessed cardiac arrest (n = 116), time from arrest to the initiation of bypass was extremely variable, with a range of 5 to 272 minutes and a mean of 45.53 ± 43.32 minutes (± standard deviation).

Bypass Performance

Successful bypass support was defined as mean blood pressure on bypass of at least 60 mm Hg and flows of 2.0 L/m^2 or more. Successful bypass support occurred in 75.4% (141/187) and flow support in 77% (144/187) of all patients.

Bypass times were also quite variable, ranging from 5 to 4,500 minutes, 36 patients having times of greater than 8 hours. Bypass initiation occurred in various areas within the hospital. The extracorporeal technologist running bypass was a perfusionist for 160 patients (85.6%), a surgeon for 7 (3.7%), a cardiologist for 1 (0.5%), a cardiac service technician for 4 (2.1%), a nurse for 5 (2.7%), other for 3 (1.6%), and unknown for 7 (3.7%). The physician placing the cannulas was a surgeon for 171 patients (91.4%), a cardiologist for 15 (8.0%), and unknown for 1 (0.5%). Six patients were transported between institutions on bypass.

Table 1. Cause of Initiation in All Arrested Patients

Cause	Witnessed	Unwitnessed
Cardiac arrest	101	10
Cardiac arrest after cardiotomy	14	. . .
Hypothermia	0	4
Pulmonary insufficiency	1	. . .
Total	116	14

Complications related to the bypass itself were relatively infrequent (Table 2), most commonly being associated with the groin cannulas. A single complication, perforation of the vena cava, led directly to a patient death.

Procedures and Weaning

Diagnostic and therapeutic procedures were accomplished during bypass in 74.9% of the patients (140/187). A variety of different diagnostic maneuvers and therapeutic procedures were performed either during emergency bypass or immediately after the patient was transferred to another form of bypass support. One third of the patients were successfully separated from bypass, and transfer to other forms of support was carried out in another third (Table 3).

Data Analysis

Generally the decision to initiate emergency bypass is made quickly and, as such, is based on only a limited number of variables. The predictive value of variables for survival was measured using relative information gain (R). Age less than versus greater than 54 years (R = 0.014), sex (R = 0.010), weight less than versus greater

Table 2. Complications Related to Bypass

Complication	No. of Patients	Percent
None	161	86.1
Technical perfusion problem—cannulas	6	3.2
Poor venous drainage	5	2.7
Bleeding at groin	2	1.1
Technical perfusion problem—circuit	2	1.1
Arterial injury	1	0.5
Equipment failure	1	0.5
Perforated vena cava	1	0.5
Other	2	1.1
Unknown	7	3.7

Table 3. Weaning From Emergency Cardiopulmonary Support

Weaning	No. of Patients	Percent
Successful wean	57	30.5
Unsuccessful wean	21	11.2
Transfer to standard bypass	43	23.0
Transfer to ventricular assist device	18	9.6
Transfer to extracorporeal membrane oxygenation	2	1.1
Bridge to transplantation	1	0.5
Not attempted	45	24.1

Table 5. Mortality Related to Time Between Cardiopulmonary Resuscitation and Bypass in Witnessed Arrests

Time	Alive >24 h	Dead
0–15 min	8	15
>15 to 30 min	6	25
>30 to 45 min	2	15
>45 to 60 min	3	14
>60 min	3	19
Unknown	1	5
Total	23	93

than 80 kg (R = 0.054), and use of inotropic support (R = 0.073) had extremely small R values, indicating essentially no predictive value. Time of cardiopulmonary resuscitation (CPR) to bypass had moderate predictive value (R = 0.359). Unwitnessed arrest, because of small sample size, did not produce a strong R value (R = 0.089). However, there were no survivors in this subgroup of patients.

Other variables were reviewed to demonstrate their relationship to outcome. Survival is considered as short term (≤30 days) and long term (>30 days) (Table 4). Cardiogenic shock patients generally fared better than those who had arrested, although in witnessed arrests, there were 17 survivors, accounting for nearly half of the long-term survivors (17/40). In patients with witnessed arrests time from arrest to bypass (Table 5) seemingly played a role in mortality with survival trends improving with shorter CPR to bypass time. The longest survivor of an arrest had a total of 221 minutes of CPR before the institution of bypass. The site of initiation of bypass did not play a major role in mortality (Table 6).

To assess the effect on patient outcome of having diagnostic and therapeutic interventions performed, survivors and nonsurvivors were grouped according to the performance of both therapeutic procedures done while on emergency bypass and those done after transfer to standard bypass. The latter period was considered to be an extension of the initial bypass, required due to the complexity of the disease process. Major therapeutic interventions were defined as those that were directed at correcting or palliating some aspect of the underlying pathology responsible for the bypass.

Table 4. Mortality by Initiating Cause

Cause	Dead on Bypass	Alive <30 Days	Alive >30 Days	Unknown
Cardiac arrest (111)	88	6	15	2
Cardiac arrest after cardiotomy (14)	12	. . .	2	. . .
Cardiogenic shock (38)	21	. . .	15	2
Cardiogenic shock after cardiotomy (6)	4	. . .	2	. . .
Hypothermia (7)	4	. . .	3	. . .
Pulmonary insufficiency (9)	5	1	3	. . .
Other (2)	1	1	. . .	. . .
Total (187)	135 (72.2%)	8 (4.3%)	40 (21.4%)	4 (2.1%)

In survivors, 77.1% (37 patients) had major intervention procedures, whereas 22.9% (11 patients) had only diagnostic procedures or bypass performed. The same comparison was made in nonsurvivors, where only half had intervention (67 versus 68 patients, respectively).

The final diagnoses of all these groups were then examined. Survivors in the interventional versus noninterventional groups were clearly different in final diagnosis:

Survivors	
Major Intervention—Group I (n = 37)	
Acute myocardial infarction	14
Coronary artery disease	7
Pulmonary embolus	4
Valve-related cardiac	3
Other cardiac	6
Trauma	2
Basal artery aneurysm	1
No Intervention—Group II (n = 11)	
Hypothermia	4
Low cardiac output syndrome (After cardiac operation, 3)	4
Pulmonary (Status asthmaticos, 1) (Smoke inhalation, 1)	2
Allergic collapse	1
Nonsurvivors	
Major Intervention—Group III (n = 67)	
Myocardial infarction	32
Pulmonary embolus	9
Valve-related	3
Coronary artery disease	3
Other cardiac	4
Trauma	7
Aortic dissection	3
Pulmonary	1
Hypothermia	1
No Intervention—Group IV (n = 68)	
Myocardial infarction	23
Coronary artery disease	1

Table 6. Mortality and Site of Bypass Initiation

Site of Initiation	Total	Dead on Bypass	Alive <30 Days	Alive >30 Days	Unknown Status
Catheterization laboratory	61	44 (72.1%)	3 (4.9%)	11 (18%)	3 (4.9%)
Operating room	53	37 (69.8%)	1 (1.9%)	14 (26.4%)	1 (1.9%)
Intensive care unit	49	36 (73.5%)	3 (6.1%)	10 (20.4%)	. . .
Emergency Dept	10	8 (80.0%)	. . .	2 (20.0%)	. . .
Floor	10	9 (90.0%)	. . .	1 (10.0%)	. . .
Other	3	1 (33.3%)	. . .	2 (66.7%)	. . .
Unknown	1	. . .	1 (1.9%)	. . .	. . .
Total	187	135	8	40	4

Valve-related	4
Arrhythmia	1
Other cardiac	8
Trauma	7
Hypothermia	5
Pulmonary embolus	5
Low cardiac output	4
Pulmonary insufficiency	4
Heart-lung transplant rejection	4
Electrocution	1
Other	5

The interventional group had more causes in which anatomically correctable disease contributed to the pathology. By contrast, in nonsurvivors, these same two groups had final diagnoses that were more comparable, though again, the noninterventional group had more causes in which direct correction of an anatomic lesion was not applicable or appropriate.

Finally, the major factors contributing to patients' death constituted the types of problems not unexpected of these moribund patients (Table 7). Neurologic status seemingly did not play a role in the decision to intervene therapeutically during bypass, in that neurologic events were distributed equally between patients having had procedures and those having only diagnostics without therapeutic maneuvers.

Comment

Emergency cardiopulmonary bypass systems have now come of age. With easily introduced, high-flow catheters, centrifugal pump systems, and simple, preassembled circuits, intervention with bypass can be carried out rapidly and efficiently in a variety of locations, both in and out of the primary hospital. Not only are perfusionists and cardiothoracic surgeons involved in the use of the systems, but medical professionals not traditionally involved with cardiopulmonary bypass, the cardiologist, emergency room physicians, nursing personnel, and respiratory therapists, have become increasingly incorporated into teams running these devices.

Table 7. Factors Contributing to Death

	Interventions (n = 67)		No Interventions (n = 68)	
Factor	No. of Patients	Percent	No. of Patients	Percent
Cardiac	48	71.6	53	77.9
Pulmonary	11	16.4	19	27.9
Central nervous system	22	32.8	15	22.1
Bleeding	19	28.4	16	23.5
Renal	0	0	1	16.2
Other	11	16.4	11	5.9

As technology expands, so do the variety of patients on whom bypass is used, placing each individual user in the position of trying to determine when the application of these systems is warranted. It was this widely variable combination of patients, users, and institutions that led to the attempt to try to separate out those patients in whom emergency systems can most appropriately be used.

Decisions to place patients on emergency portable bypass systems are often made quickly. Those few data points that are often readily available to the treating "bypass" physician were examined. In reviewing these few factors, age, sex, size, and the use of prebypass inotropes were not found to be strong indicators of potential mortality. Of great concern is the use in patients in whom cardiac arrest has occurred. Patients with witnessed cardiac arrest have had some success in resuscitation. Although mortality is high, a number of patients (17) survived to leave the hospital who otherwise might have died. This is in contradistinction to the observation of others [9]. In this setting, unwitnessed arrest is clearly a cautious indicator against the use of emergency bypass systems. This is similar to the findings of other authors [9]. Although not noted in the present set of Registry patients, unwitnessed arrest in the presence of profound accidental hypothermia is still a potential area for the use of emergency bypass [12, 13].

The time from witnessed arrest to bypass, ie, length of CPR, was quite variable. However, as time of CPR to bypass increased, mortality generally increased. This had moderate predictive value for mortality and should not be a major consideration for withholding bypass if evidence of neurologic function persists. This is somewhat at odds with other authors (Hartz and associates [9]), who suggest 30 minutes as a cutoff for bypass initiation. Arrested

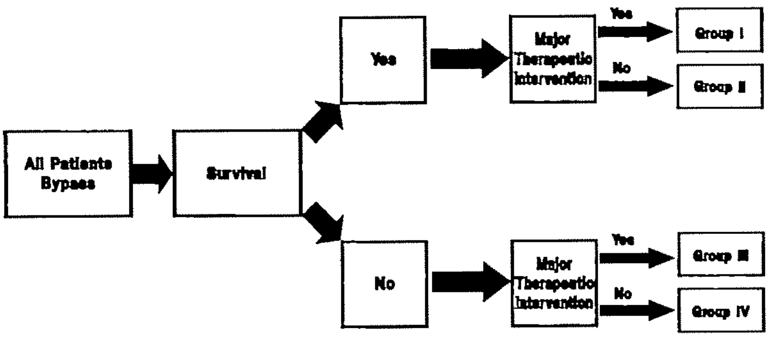


Fig 2. Interventional implications and mortality: Division of patients into groups of survivors or nonsurvivors, and subsequently into groups based on major therapeutic interventions, allows the final diagnostic categories to be compared as four separate entities.

patients, as expected, had a higher level of mortality than nonarrested patients.

Of the survivors, the number placed on bypass within the cardiac catheterization laboratory was not significant, indicating that this location did not play a role in improving survival. This is different than the findings of Mooney and co-workers [10], in which those in the catheterization laboratory had improved survival. However in that study, the clinical investigators were clearly prepared to use emergency bypass in patient salvage and had excellent outcome.

The ability to correct the underlying pathology seemingly plays a role in patient survival. This is suggested by a variety of authors [6, 8, 10, 14]. It becomes apparent that the time on bypass was either therapeutic in and of itself, or used to support the patient until appropriate palliative or corrective interventions could be carried out (Fig 2).

Group I patients had underlying correctable pathologies, generally approachable anatomically, and clearly benefited from the time bypass gave for therapeutic corrections to be performed, consistent with the emphasis Phillips and colleagues [5] made in 1983. Of these patients, some were transferred to standard bypass to carry out the corrective maneuvers, again emphasizing the role that emergency bypass played in providing time to support the patient in preparation for appropriate interventions. These final diagnoses in group I are contrasted with group II patients. Here the pathologies were not "anatomic" and the time on bypass was seemingly therapeutic in itself. Hypothermia, low cardiac output syndrome, drug-related problems, and pulmonary insufficiency were common. The time of support assisted the patient long enough for the underlying pathology to be improved without major corrective operation or interventions.

Group III patients, nonsurvivors similar in final diagnoses to group I, were seemingly beyond the point of salvage because of the severity of structural disease and probable metabolic abnormalities. Combining group I (n = 37) and group III (n = 67), therapeutic intervention led to a 35.6% (37/104) survival rate.

Finally, patients in group IV, nonsurvivors who have had no major interventions, were examined. Pathologies without specific underlying anatomic causes are again common. Combining groups II (n = 11) and IV (n = 68) yields an overall survival of 13.9% (11/79), implying that the achievement of survival in nonanatomic processes is more difficult. In group IV patients, decisions were made, on unknown factors, to pursue bypass. However, no attempts were made to correct underlying pathologies. With the low overall survival in group IV patients, major diagnostic categories or clinical indicators may ultimately be found in these patients that will mitigate against the initiation of bypass.

Emergency bypass systems can make a difference in survival. Absolute indicators for initiating or withholding bypass are still elusive. Patients with unwitnessed arrest, unless associated with other extraordinary circumstances (ie, profound accidental hypothermia) are poor candidates. Prolonged CPR time of more than 30 minutes is a moderate contraindication to bypass. However, the ability to perform therapeutic interventions positively affects patient survival, and the ability to potentially do so is a good indicator for emergency bypass initiation or continuation. Patients with anatomically correctable problems are good candidates for bypass and potential salvage.

The group of patients with "nonanatomic" pathology, ie, hypothermia, reversible pulmonary disease, or low output syndromes, benefit from bypass alone, allowing time to correct underlying metabolic and physiologic problems. Although candidates for attempted resuscitation, these patients' overall survival is less than those with interventionally amenable disease.

Emergency portable bypass use is expanding. On the horizon are more compact, technically improved systems. Portability means that intrahospital and interhospital transport can be carried out safely and effectively. The advent of heparin-bonded tubing, oxygenator, pump heads, and cannulas opens the door to candidates for cardiopulmonary bypass systems, particularly those with trauma and intracranial malformations, in whom heparinization was previously contraindicated [12, 15]. By continuing to combine multiinstitutional data, stronger and more specific indicators for emergency bypass use will hopefully be clarified, improving the ability of the treating physician to resuscitate and salvage a subset of extremely ill patients.

The National Cardiopulmonary Support Registry for Emergent Applications is indebted to Judy McDonald and Leona Hempel for their excellent assistance and to William Sacco, PhD, and Wayne Coopes, PhD (Trianalytics, Inc, Bel-Air, MD), for their analysis, review, and expertise.

References

1. Gibbon JH. The maintenance of life during experimental occlusion of the pulmonary artery followed by survival. Surg Gynecol Obstet 1939;69:602–14.
2. Cooley DA, Beall AC. A technique of pulmonary embolectomy using temporary cardiopulmonary bypass: experimental and clinical considerations. J Cardiovasc Surg 1961;2: 469–76.
3. Mattox KL, Beall AC. Applications of portable cardiopulmonary bypass to emergency instrumentation. Med Instrum 1977;11:347–9.
4. Mattox KL, Beall AC. Resuscitation of the moribund patient using portable cardiopulmonary bypass. Ann Thorac Surg 1976;22:436–42.
5. Phillips SJ, Ballent B, Slonine D, et al. Percutaneous initiation of cardiopulmonary bypass. Ann Thorac Surg 1983;36:223–5.
6. Phillips SJ, Zeff RH, Kongtahworn C, et al. Percutaneous cardiopulmonary bypass: application and indication for use. Ann Thorac Surg 1989;47:121–3.
7. Raithel SC, Swartz MT, Braun PR, et al. Experience with an emergency resuscitation system. Trans Am Soc Artif Intern Organs 1989;35:475–7.
8. Reichman RT, Joyo CI, Dembitsky WP, et al. Improved patient survival after cardiac arrest using a cardiopulmonary support system. Ann Thorac Surg 1990;49:101–5.
9. Hartz R, LoCicero J III, Sanders JH Jr, Frederiksen JW, Joob AW, Michaelis LL. Clinical experience with portable cardiopulmonary bypass in cardiac arrest patients. Ann Thorac Surg 1990;50:437–41.
10. Mooney MR, Arom KV, Joyce LD, et al. Emergency cardiopulmonary bypass support in patients with cardiac arrest. J Thorac Cardiovasc Surg 1991;101:450–4.
11. Champion HR, Sacco WJ, Carnazzo AJ, et al. The trauma score. Crit Care Med 1981;9:672–6.
12. Von Segesser LK, Garcia E, Turina M. Perfusion without systemic heparinization for rewarming in accidental hypothermia. Ann Thorac Surg 1991;52:560–1.
13. Laub GW, Banaszak D, Kupferschmid J, Magovern GJ, Young JC. Percutaneous cardiopulmonary bypass for the treatment of hypothermic circulatory collapse. Ann Thorac Surg 1989;47:608–11.
14. Phillips SJ. Percutaneous cardiopulmonary bypass and innovations in clinical counterpulsation. Crit Care Clin 1986;2: 297–318.
15. Bennett J, Hill J, Bruhn P, Long W, Parsons J. Heparin-free cardiopulmonary support, utilizing a Carmeda coated circuit, for a patient with pulmonary hemorrhage and multiple trauma. Proceedings of the International Conference of AmSECT, March 2–4, 1991:89–92.

Appendix 1. Contributing Centers

Emanuel Hosital and Health Center: Jonathan G. Hill, MD*, Pamela S. Bruhn, BSN, RN, William B. Long, MD; **The Appleton Heart Institute**: Paul Askari, CCP*; **Harper Hospital/Wayne State University**: Frank A. Baciewicz, Jr, MD*, Brian Paules, CPT; **Johns Hopkins Hospital**: Candace L. Banchieri, CCP*; **Community Hospitals Central California**: Sheldon E. Cohen, MD*, Alan Lummis, Denise Belknap, RN; **Dartmouth-Hitchcock Medical Center**: Gordon R. DeFoe, CCP*; **St. Elizabeth's Hospital**: James Filipich*; **Southwest Memorial Hospital**: Michael Gallagher, MD*; **Sacred Heart Hospital**: David German, CCP, PA*; **The Emory Clinic of Crawford W. Long Memorial Hospital**: Robert A. Guyton, MD*, Candace Parker-Steele, CCT, CCP; **Scott and White Memorial Hospital**: F. L. Korompai, MD*; **Humana of San Antonio**: Charles Moore, MD*; **Milton S. Hershey Medical Center/Pennsylvania State University**: Walter E. Pae, Jr, MD*, Cynthia A. Miller, BS, William S. Pierce, MD, John L. Myers, MD; **Stritch School of Medicine/Loyola University**: Roque Pifarre, MD*; **Butterworth Hospital**: Dr Luis Tomatis*, Dick Kanten, RN, CCP; **Christ Hospital and Medical Center**: Zev Davis, MD*; **Marquette General Hospital**: Libby Blichfeldt, CCP.

Appendix 2. Questions Formatted Into National Cardiopulmonary Support Registry

- Demographics
  - Age, sex, weight
- Cause
  - Cause of initiation of bypass (cardiac arrest, cardiogenic shock, hypothermia, pulmonary insufficiency)
  - Prebypass illness
  - Prebypass inotropic support
  - Final diagnosis
- Bypass Data
  - Site of initiation
  - Transport on bypass
  - Site of cannulation
  - Physician placing cannulas
  - Technologist running bypass (surgeon, perfusionist, nurse, cardiologist, other)
  - Size and type of cannulas
  - Circuit type
  - Activated clotting time target range
  - Time on bypass
  - Support on bypass (mean blood pressure, flow)
  - Complications of bypass
- Procedures
  - Intraaortic balloon pump used, when
  - Procedures done on bypass
  - Procedures done immediately after bypass
- Weaning
  - Successful
  - Transfer to other support (ventricular assist device, standard bypass, extracorporeal membrane oxygenation)
- Status
  - Alive ≤30 days
  - Alive >30 days
  - Death on bypass or within 24 hours
- Factors Contributing to Death
  - Neurologic
  - Bleeding
  - Renal
  - Cardiac
  - Other

---

* Principal investigator.

Effect of Light Dose on the Photodynamic Destruction of Endobronchial Tumors

James S. McCaughan, Jr, MD, Philip C. Hawley, MD, David G. Brown, MD, Gerard S. Kakos, MD, and Thomas E. Williams, Jr, MD

Laser Medical Research Foundation, Columbus, Ohio

The effects of various light power densities (milliwatts per centimeter of diffusing fiber [mW/cf]) and light doses (joules per centimeter of diffusing fiber [J/cf]) on the effectiveness of photodynamic therapy to endobronchial and tracheal tumors were evaluated at 46 different sites. All patients had squamous cell carcinoma or adenocarcinoma. They received 2 mg/kg body weight dihematoporphyrin ether intravenously 2 days before treatment bronchoscopy. Only one light treatment was delivered to the site. Patients were treated with diffusing cylinder light tips and underwent toilet bronchoscopy 2 days after photodynamic therapy. The percentage of obstruction was estimated before and after treatment and before and after toilet bronchoscopy. There was no difference between the effects resulting from power densities of 400 and 500 mW/cf, nor were there differences in the reactions between squamous cell carcinoma and adenocarcinoma. The amount of tumor that could be removed at the end of the treatment bronchoscopy, the amount of reobstruction by secretions and exudate seen at toilet bronchoscopy, and the final percent decrease in obstruction at the end of toilet bronchoscopy were proportional to the light dose. Because the final percentage decrease in obstruction plateaued at light doses of 400 to 500 J/cf and there was no statistically significant difference between 400 and 500 J/cf, we recommend using a power density of 500 mW/cf and a light dose of 400 J/cf during photodynamic therapy.

(Ann Thorac Surg 1992;54:705–11)

Since 1982, we have conducted an ongoing study of the efficacy of photodynamic therapy (PDT) to treat endobronchial tumors in patients with primary or metastatic obstructive disease. During this time, 81 patients have received PDT to 324 sites using 175 treatment bronchoscopies. Some of these patients with stage III lung cancer have survived more than 5 years. Patients with tumor in situ have survived more than 6 years [1–7].

As our experience increased, various techniques for light delivery, power density measurements, light doses, and the time interval between injection and therapy were evaluated and modified. Clinically it became obvious that tumor could be removed at the end of the treatment bronchoscopy and that the amount of tumor removed increased with the amount of light given during treatment. It also became obvious that higher light doses created more exudate and secretions after the treatment, with subsequent reobstruction of the bronchus seen at toilet bronchoscopy 2 days after treatment. Removal of this and any remaining tumor is an integral part of the therapy regimen.

We reviewed the immediate results of PDT on tumors to determine the effects of different light doses.

Material and Methods

All eligible patients had biopsy-proven obstructive squamous cell carcinoma or adenoendobronchial carcinoma and had received or were ineligible for conventional operation, radiotherapy, or both. Frequently it was necessary to treat several adjacent sites because of the extent of the disease. As this may cause overlap of light exposure, we compared patients who received only one treatment at a particular site.

Two days before treatment bronchoscopy, all patients received intravenously dihematoporphyrin ether (Lederle, Pearl River, NY) in a dose of 2 mg/kg body weight.

The 630-nm light for the treatment was generated by a tunable dye argon laser (model 171; Spectra Physics, Mt View, CA) system and was delivered through quartz fibers passed down the biopsy channel of the fiberoptic bronchoscope. The distal 1 to 2.5 cm of the fibers were modified to deliver the light perpendicular to the axis of the fiber (Laserguide, Santa Barbara, CA; or Lederle). The Laserguide diffusing tips were 1 mm thick and the Lederle diffusing tips were 1.8 mm thick. Both types of fiber tips delivered homogenous light along their length.

When possible, the diffusing fiber was inserted directly into the tumor (interstitial). When the tumor was too hard, flat, or concentric to allow direct insertion, the fiber was placed adjacent to the tumor for surface irradiation (surface). Before and after treatment, power densities per centimeter of fiber tip diffuser (mW/cf) were calculated by dividing the length of the diffuser tip into the total power output measured with an integrating sphere radiometer (Laserguide). The power delivered through the fiber during the treatment was continuously monitored with a "leakage meter" (Laser Medical Research Foundation,

---

Accepted for publication Feb 18, 1992.

Address reprint requests to Dr McCaughan, 323 East Town St, Columbus, OH 43215.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Percent Obstruction Before Photodynamic Therapy and After Toilet Bronchoscopy

Site	No. Sites	Mean % Obstruct Before PDT	Mean % Obstruct After Toilet Bronchoscopy	Mean Decrease % Obstruct	*p* Value (*t* test)
All sites	46	65	19	46	<0.001
Trachea	7	43	19	24	0.050
All bronchi	39	67	19	48	<0.001
200 J/cf	8	54	25	24	0.005
300 J/cf	4	64	23	41	0.056
400 J/cf	9	59	15	31	0.001
500 J/cf	13	78	20	58	<0.001
Squamous	30	69	19	50	<0.001
Adeno	9	62	19	43	<0.001

PDT = photodynamic therapy.

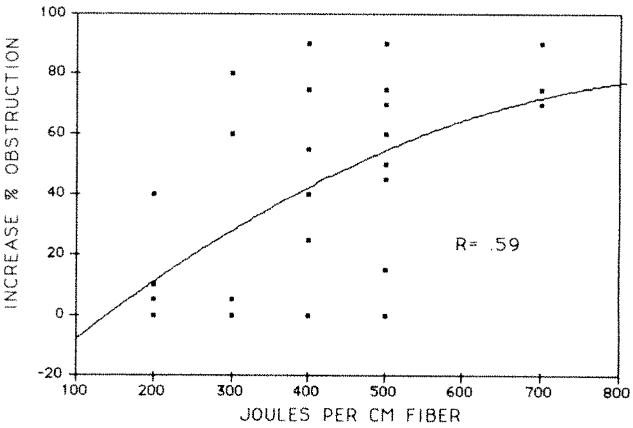


Fig 2. Increase of percent obstruction seen at beginning of toilet bronchoscopy (compared with the percent obstruction remaining at end of photodynamic therapy) as a function of light dose (J/cm fiber). Correlation coefficient = 0.59.

Columbus, OH). The wavelength was checked before and after treatment with a spectrometer (model H-20; Instruments SA, Metuchen, NJ).

At the end of the treatment bronchoscopy, as much of the tumor as possible was mechanically removed. A toilet bronchoscopy was performed 2 days after the treatment bronchoscopy, and again as much tumor as possible was mechanically removed.

The percentage of observed obstruction and diameter of the opening at the sites were estimated before and after treatment and before and after toilet bronchoscopy by comparing them with the bronchoscope (6 mm) and biopsy forceps and the diameter of the normal bronchus at the obstruction.

We compared the effects of power densities of 400 mW/cf and 500 mW/cf using the same light dose. We compared the effects of light doses of 200, 300, 400, 500, 600, and 700 joules per centimeter of diffusing fiber tip (J/cf). We calculated (1) the decrease of percent obstruction at the end of treatment, defined as the percentage of obstruction at the beginning of treatment minus the percentage of obstruction after treatment; (2) the increase of percent obstruction at toilet bronchoscopy, defined as the percentage of obstruction at the beginning of the toilet bronchoscopy minus the percentage of obstruction at the end of treatment bronchoscopy; (3) the decrease of percent obstruction after toilet bronchoscopy, defined as the percentage of obstruction at the beginning of PDT treatment bronchoscopy minus the percentage of obstruction at the end of toilet bronchoscopy; and (4) the percent decrease of obstruction after toilet bronchoscopy, defined as the percentage of obstruction at the beginning of treatment minus the percentage of obstruction after toilet bronchoscopy divided by the percentage of obstruction at the beginning of treatment.

The computer statistical program STATWORKS (Cricket, 1985) was used to generate regression curves. A correlation coefficient was considered moderate between 0.3 and 0.6 and marked above 0.6.

Paired and unpaired Student's *t* tests were used to

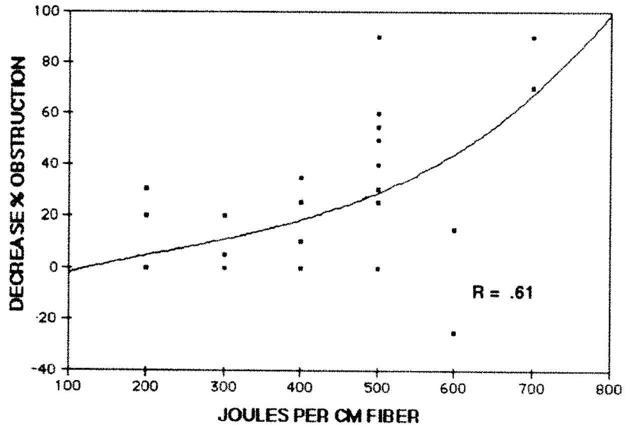


Fig 1. Decrease of percent obstruction at the end of photodynamic therapy for all bronchi treated as a function of the light dose (J/cm fiber). Correlation coefficient = 0.61.

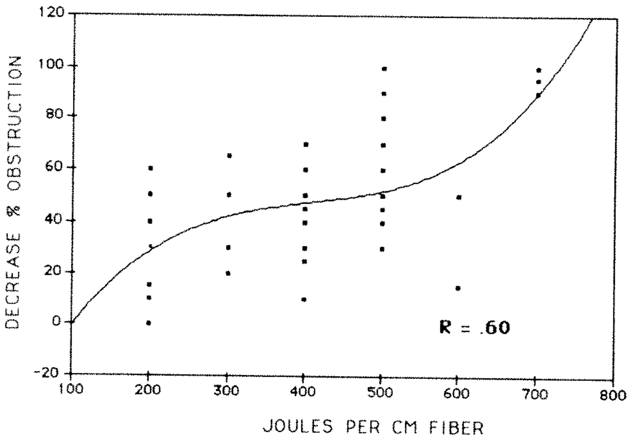


Fig 3. Decrease of percent obstruction after toilet bronchoscopy (as compared with percent obstruction before photodynamic therapy) for all bronchi as a function of light dose (J/cm fiber). Correlation coefficient = 0.60.

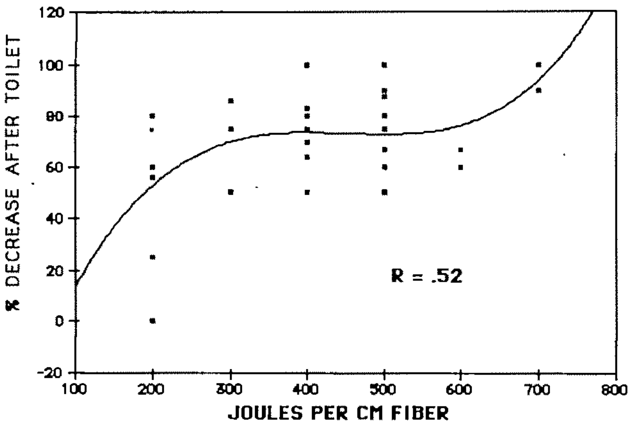


Fig 4. Decrease of percent obstruction of all bronchi after toilet bronchoscopy from percent obstruction before photodynamic therapy as a function of light dose (J/cm fiber). Correlation coefficient = 0.52.

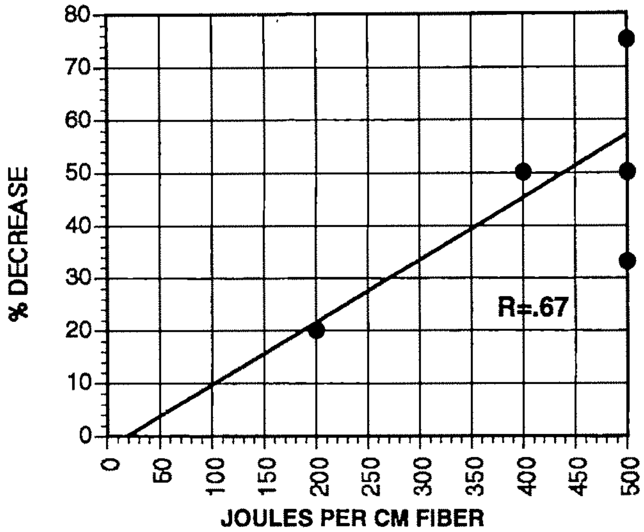


Fig 5. Decrease of percent obstruction at end of toilet bronchoscopy (as compared with percent obstruction before photodynamic therapy) for tracheal tumors as a function of light dose (J/cm fiber). Correlation coefficient = 0.67.

determine probabilities. A p value less than 0.05 was considered statistically significant. Because of insufficient data points for light doses of 600 and 700 J/cf, we could compare only the effects of 200, 300, 400, and 500 J/cf statistically.

Results

After eliminating sites that received treatments to adjacent areas (and thereby possible overlap of irradiation), 46 sites were evaluated (37 squamous, 9 adenoendobronchial). Of the sites found to have squamous tumors, the bronchi affected were as follows: 2 left lower lobe, 5 left main bronchus, 5 left upper lobe, 4 right intermediate, 1 right lower lobe, 9 right main bronchus, 4 right upper lobe, and 7 trachea. All adenocarcinomas were located in the right main bronchus.

Table 1 presents the average percent obstruction before PDT treatment and after toilet bronchoscopy for all sites and for different light doses administered to the bronchi. The average percent obstruction for all sites decreased from 65% before PDT treatment to 19% after toilet bronchoscopy. According to the paired Student's t tests, the decrease in the amount of obstruction of the bronchi was statistically significant in all light doses except for 300 J/cf ($p = 0.56$), although its average percent obstruction decreased from 64% to 23%. Because only four observations were made at this light dose, the Student's t test for 300 J/cf is probably not reliable.

Color plate 1 shows complete obstruction of the right main bronchus by adenocarcinoma and the opening obtained at the end of PDT using 500 mW/cf to deliver 400 J/cf. The left lower corner shows complete reocclusion by exudate 2 days after PDT. The right lower corner shows the opening obtained at the end of the toilet bronchoscopy, and the center picture shows the area 10 months later.

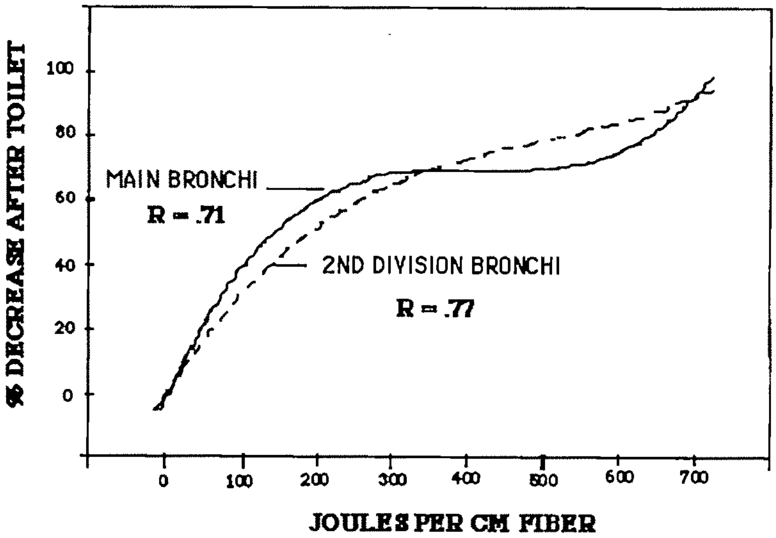
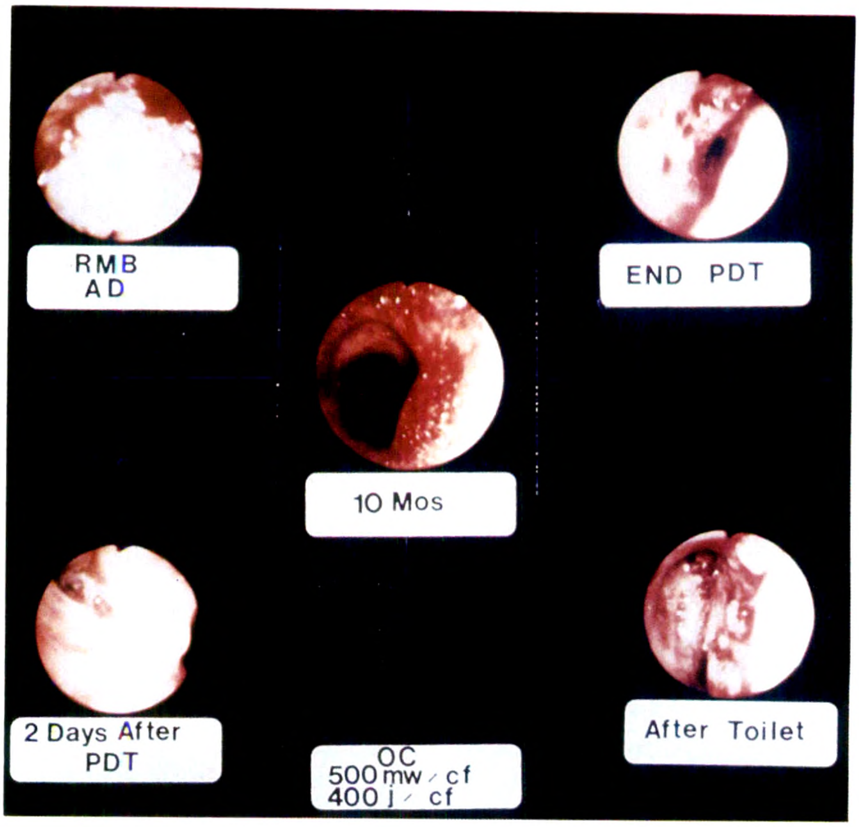


Fig 6. Percent decrease obstruction after toilet bronchoscopy (as compared with percent obstruction before photodynamic therapy) for main bronchi and second division bronchi as a function of light dose (J/cm fiber). Main bronchi correlation coefficient = 0.71; second division bronchi correlation coefficient = 0.77.



Color plate 1. Complete obstruction of the right main bronchus (RMB) by adenocarcinoma (AD) and the opening obtained at the end of photodynamic therapy (PDT) using 500 mW/cf to deliver 400 J/cf. The left lower corner shows complete reocclusion by exudate 2 days after PDT. The right lower corner shows the opening obtained at the end of the toilet bronchoscopy, and the center picture shows the area 10 months later.

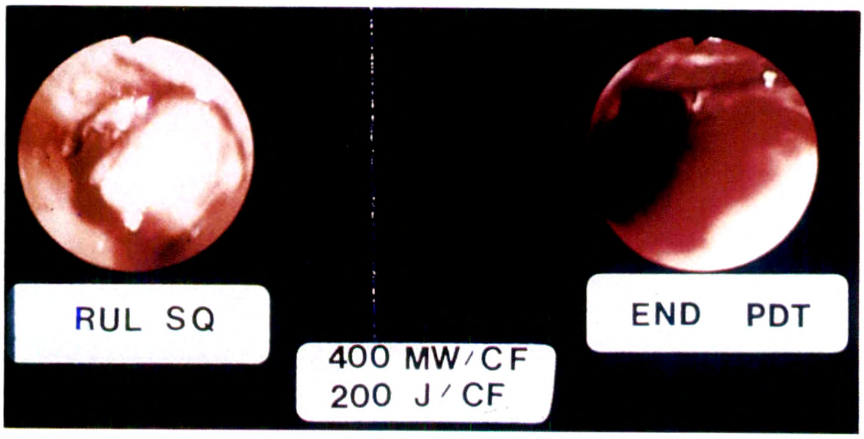
Effects on Squamous Cell Versus Adenocarcinoma

The mean light doses for the 30 bronchial squamous sites and 9 adenocarcinoma sites were 400 J/cf and 467 J/cf, respectively; the mean percent decrease in obstruction after toilet bronchoscopy was 50% for squamous and 43% for adenocarcinoma. Seven squamous and seven adenocarcinoma main bronchial sites were treated with 500 J/cf. The mean percent obstruction before treatment was 65% for adenocarcinoma and 69% for squamous cell. The mean percent obstruction after toilet bronchoscopy was 16% for adenocarcinoma and 19% for squamous cell. The mean decrease in percent obstruction after toilet bronchoscopy was 73% for squamous cell tumors and 72% for adenocarcinoma. Thus, the type of tumor did not affect the ability of the PDT to remove the obstruction ($p = 0.805$).

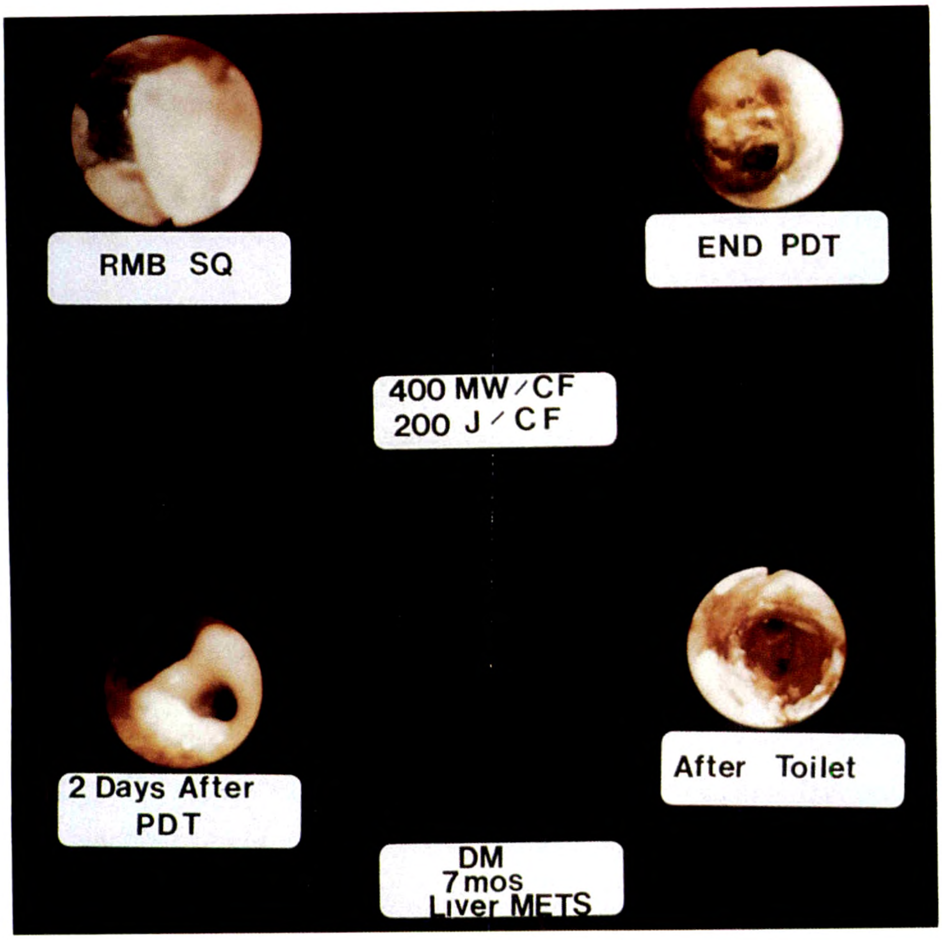
Effect of Different Light Doses

DECREASE OF OBSTRUCTION AT END OF TREATMENT BRONCHOSCOPY. A regression curve for the decrease of percent obstruction at the end of PDT treatment bronchoscopy as a function of the light dose for all bronchial sites treated is presented in Figure 1. The correlation coefficient is 0.61. With higher light doses more tumor can be removed at the end of treatment.

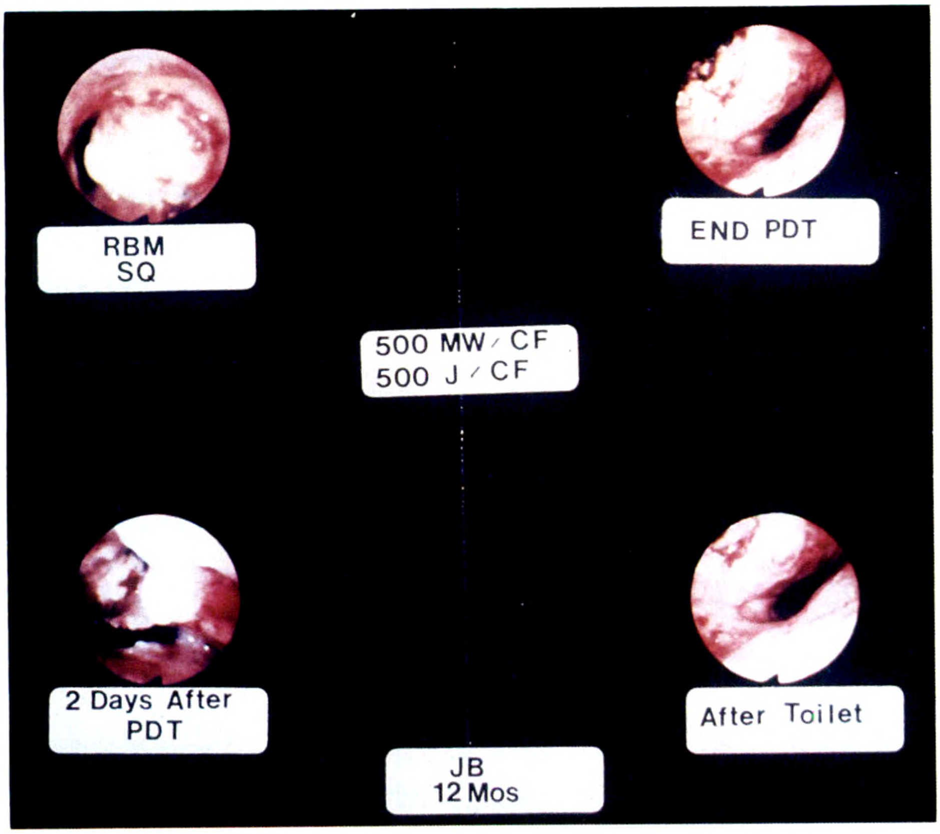
Color plate 2 shows almost complete obstruction of the right upper lobe by squamous cell cancer before treatment



Color plate 2. Almost complete obstruction of the right upper lobe (RUL) by squamous cell cancer (SQ) and the resulting almost complete opening by removal of tumor at the end of the photodynamic therapy (PDT) treatment bronchoscopy using 400 mW/cf to deliver 200 J/cf.



Color plate 3. Complete obstruction of the right main bronchus (RMB) *by squamous cell cancer* (SQ). *The area was treated with 400 mW/cf to deliver 200 J/cf. The right upper corner shows the opening obtained by removing tumor at the end of the treatment. The left lower corner shows the exudate that occurs and reobstructs the bronchus as seen 2 days after photodynamic therapy* (PDT). *The right lower corner shows the opening obtained at the end of the toilet bronchoscopy. The patient died 7 months later of liver metastases* (METS) *but was having no difficulty breathing.*



Color plate 4. Complete obstruction of the right main bronchus (RMB) *by squamous cell carcinoma* (SQ). *The right upper corner shows the opening obtained at the end of photodynamic therapy* (PDT) *using 500 mW/cf to deliver 500 J/cf. The left lower corner shows the edema and reaction seen 2 days after PDT, and the right lower corner shows the opening after exudate and residual tumor were removed. The patient died of extrinsic compression of the bronchus.*

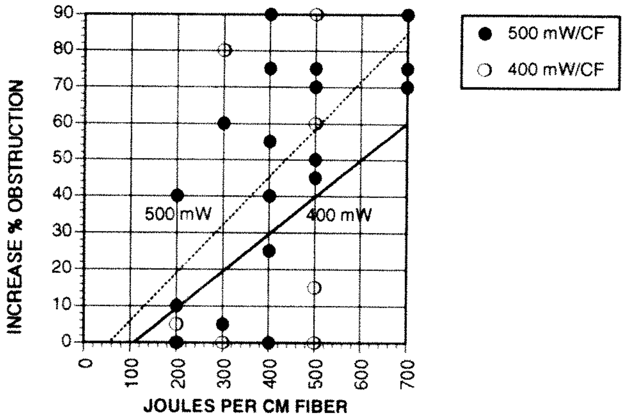


Fig 7. Comparison of increase of percent obstruction seen at toilet bronchoscopy as a function of power density and light dose. Coefficient correlation for 400 mW/cf = 0.39; correlation coefficient for 500 mW/cf = 0.61.

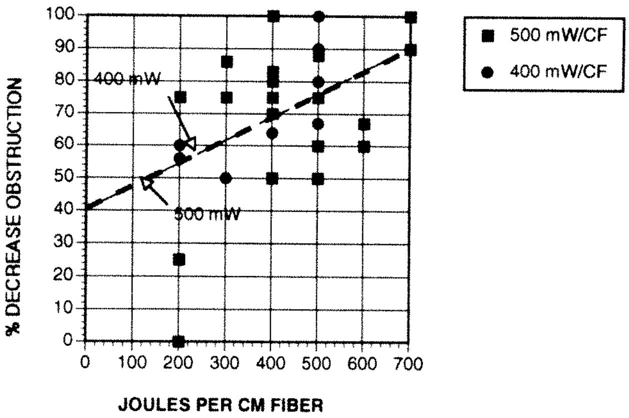


Fig 9. Comparison of percent decrease of obstruction at end of toilet bronchoscopy as a function of power density and light dose. Correlation coefficient for 400 mW/cf = 0.41; correlation coefficient for 500 mW/cf = 0.39. The curves are identical.

and almost complete opening after removal of tumor after treatment bronchoscopy using 400 mW/cf to deliver 200 J/cf.

INCREASE OF OBSTRUCTION AT TOILET BRONCHOSCOPY. A regression curve for the increase of percent obstruction by the exudate and secretions that occur after PDT treatment bronchoscopy is shown in Figure 2. The correlation coefficient is 0.59. Unfortunately, higher light doses also result in a greater degree of reobstruction after treatment, and this material must be removed by toilet bronchoscopy.

Color plate 3 shows complete obstruction of the right main bronchus by squamous cell cancer. The area was treated with 400 mW/cf to deliver 200 J/cf. The opening obtained by removing tumor at the end of the treatment is shown in the upper right corner. The left lower corner shows the exudate that reobstructs, as seen 2 days after PDT. The right lower corner shows the opening obtained at the end of the toilet bronchoscopy. The patient died 7 months later of liver metastases but was having no difficulty breathing.

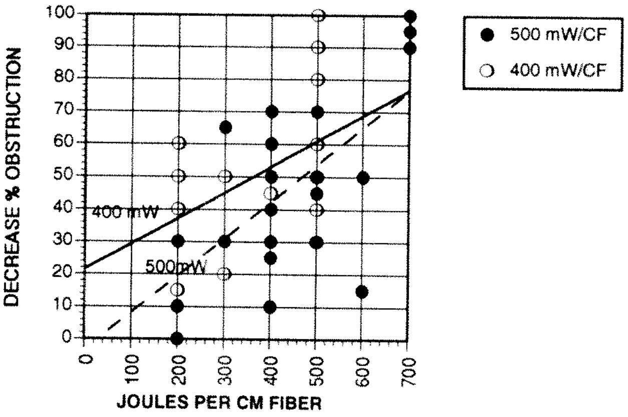


Fig 8. Comparison of decrease of percent obstruction after toilet bronchoscopy as a function of power density. Correlation coefficient for 400 mW/cf = 0.40; for 500 mW/cf = 0.54.

DECREASE OF OBSTRUCTION AT END OF TOILET BRONCHOSCOPY. The decrease of obstruction of the bronchi before PDT and after toilet bronchoscopy is shown in the regression curve with a correlation coefficient of 0.60 (Fig 3).

The regression curve derived from the calculated percent decrease in obstruction after toilet bronchoscopy from the percent obstruction before PDT for treatments plotted for all the bronchi had a correlation coefficient of 0.52 (Fig 4). The percent decrease of obstruction after toilet bronchoscopy increased as the light dose increased up to 400 to 500 J/cf.

Because the trachea and the bronchi have quite dissimilar diameters (trachea, 14 to 22 mm; main bronchi, 8 to 9 mm; and second division bronchi, 6 to 7 mm), we compared the effect of different light doses on the sites. The main bronchi were the left and right main bronchi. The second-division bronchi were right upper lobe, right intermediate bronchus, right lower lobe, left upper lobe, and left lower lobe. The regression curve derived from the effect of different light doses on the percent decrease of obstruction of the trachea after toilet bronchoscopy from the percent obstruction before PDT had a correlation coefficient of 0.67 (Fig 5). The regression curves for the percent decrease of obstruction after toilet bronchoscopy from the percent obstruction before PDT for the main bronchi and the second-division bronchi as a function of the light dose per centimeter of fiber were essentially identical (Fig 6).

Color plate 4 shows complete obstruction of the right main bronchus by squamous cell carcinoma. The right upper corner shows the opening obtained at the end of PDT using 500 mW/cf to deliver 500 J/cf. The left lower corner shows the edema and reaction seen 2 days after PDT, and the right lower corner shows the opening after this exudate and residual tumor were removed. The patient died of extrinsic compression of the bronchus.

The probabilities of any difference in the calculated mean percent decrease in obstruction after toilet bronchoscopy from the percent obstruction before PDT when 200, 400, and 500 J/cf were used were evaluated with the unpaired Student's *t* test. There was no statistical difference in the percent decrease of obstruction after toilet bronchoscopy when 400 J/cf was compared with 500 J/cf ($p = 0.999$). There was a significant difference when 200 J/cf was compared with 400 J/cf ($p = 0.050$), 500 J/cf ($p = 0.044$), or combined 400 and 500 J/cf ($p = 0.016$).

Effect of Different Light Power Densities

Sixteen bronchial sites were treated with a power density of 400 mW/cf, and 23 sites were treated with a power density of 500 mW/cf. Regression curves that compare the increase of percent obstruction seen at toilet bronchoscopy from the percent obstruction at the end of PDT bronchoscopy for all the bronchi using various light doses with power densities of 400 mW/cf (correlation coefficient = 0.39) and 500 mW/cf (correlation coefficient = 0.61) are shown in Figure 7. Regression curves that compare decrease in percent obstruction after toilet bronchoscopy from the percent obstruction before PDT bronchoscopy for various light doses with power densities of 400 mW/cf (correlation coefficient = 0.41) and 500 mW/cf (correlation coefficient = 0.54) are shown in Figure 8. The decrease of percent obstruction before PDT after toilet bronchoscopy is shown in Figure 9 for 400 mW/cf (correlation coefficient = 0.41) and 500 mW/cf (correlation coefficient = 0.39). The curves actually fall on the same line.

Comment

A limiting factor in the effectiveness of PDT is the ability of the 630 nm light to penetrate only 5 to 10 mm. Because the maximum diameters of the main bronchi and trachea are 9 mm and 22 mm, respectively, PDT is ideally suited for treating obstruction due to endobronchial tumors. Using joules per centimeter of diffusing fiber as the parameter for light dose measurement is satisfactory when treating the bronchi or other small tubular structures, such as the bile ducts [8].

Based on our study, the following conclusions can be made about PDT when delivered 2 days after injection with dihematoporphyrin ether: Photodynamic therapy is equally effective in destroying and removing adenocarcinomas and squamous cell carcinomas. Results are equal whether power densities of 400 mW/cf or 500 mW/cf are used to deliver the same total light dose; 500 mW/cf can be used because this dose decreases treatment time. Tumor can be removed at the end of the treatment; the amount that can be removed increases as the light dose is increased. The amount of reobstruction of the bronchus by exudate and secretions after treatment bronchoscopy increases as the light dose increases. As a result, a toilet bronchoscopy is an integral part of the treatment regimen and must be performed, even if tumor is removed at the end of the treatment bronchoscopy. The effectiveness of destruction and removal of endobronchial tumors increases as the light dose increases up to a plateau of 400 to 500 J/cf. There was a statistically significant increase in the amount of tumor removed with 400 J/cf or 500 J/cf, as compared with 200 J/cf. The same light dose is less effective for tracheal tumors than for bronchial tumors because the larger diameter of the trachea causes a decreased light dose per square centimeter of tumor surface exposed.

References

1. McCaughan JS Jr, Williams TE Jr, Bethel BH. Photodynamic therapy of endobronchial tumors. Lasers Surg Med 1986;6:336–45.
2. McCaughan JS Jr, Hawley PC, Walker J. Management of endobronchial tumors: a comparative study. Semin Surg Oncol 1989;5:38–47.
3. Edell ES, Cortese DA. Bronchoscopic phototherapy with hematoporphyrin derivative for treatment of localized bronchogenic carcinoma: a 5-year experience. Mayo Clin Proc 1987;62:8–14.
4. Balchum OJ, Doiron DR. Photoradiation therapy of endobronchial lung cancer. Clin Chest Med 1985;6:255–75.
5. Lam S, Muller NL, Miller RR, et al. Predicting the response of obstructive endobronchial tumors to photodynamic therapy. Cancer 1986;58:2298–306.
6. McCaughan JS Jr, Barabash RD, Penn GM, Glavan BJ. Nd: YAG laser and photodynamic therapy for esophageal and endobronchial tumors and under general and local anesthesia. Effects on arterial blood gas levels. Chest 1990;98:1374–8.
7. Dougherty TJ. Photosensitization of malignant tumors. Semin Surg Oncol 1986;2:24–37.
8. McCaughan JS, Mertens BF, Cho C, Barabash RD, Payton HW. Photodynamic therapy to treat tumors of the extrahepatic biliary ducts. Arch Surg 1991;126:111–3.

Nicardipine: Myocardial Protection in Isolated Working Hearts

Marc E. Mitchell, MD, David A. DeBoer, MD, Michael D. Crittenden, MD, and Richard E. Clark, MD

Surgery Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

The effectiveness of the calcium antagonist nicardipine in protecting the ischemic myocardium was evaluated using the hemodynamic recovery of isolated working rat hearts subjected to hyperkalemic cardiac arrest followed by ischemia at 37.5°C and 10°C. Rat hearts (n = 51) received 20 mL of cardioplegia and were subjected to 27 minutes of ischemia at 37.5°C. Group A (control) did not receive nicardipine. Groups B through F received nicardipine in the cardioplegia with total doses ranging from 2 μg to 6 μg. Group A had 46% survival of ischemia, whereas groups C (3 μg) and D (4 μg) had survival rates of 88% and 100%, respectively ($p < 0.05$). The recovery of aortic flow after ischemia was 35% in group A, compared with 76% in group B (2 μg) and 81% in group D ($p < 0.05$). Group A had 49% postischemic recovery of cardiac output, whereas groups B and D had 82% and 85% recovery ($p < 0.05$). The postischemic recovery of stroke volume was 48% in group A compared with 84% in group B, 87% in group D, and 73% in group E (5 μg) ($p < 0.05$). Additional rats were exposed to 210 minutes of ischemia (n = 41) or 240 minutes of ischemia (n = 56) at 10°C. Control groups did not receive nicardipine, whereas treatment groups received nicardipine in the cardioplegia with total doses ranging from 1.4 μg to 6.4 μg. There were no significant differences in the survival of ischemia or the recovery of function after ischemia at 10°C. We conclude that nicardipine offers significant protection to the ischemic rat myocardium at normothermia, with an optimal dose of 2 to 4 μg. We have been unable to demonstrate any beneficial effect from the administration of nicardipine at 10°C.

(Ann Thorac Surg 1992;54:712–6)

Hypothermic potassium cardioplegia is used to protect the myocardium during the ischemic period of aortic cross-clamping. Alterations in the transmembrane flux of calcium ions are partially responsible for the myocardial injury that occurs during ischemia and reperfusion. Calcium accumulates in the mitochondria and sarcoplasmic reticulum during ischemia, resulting in an acceleration of the degradation of adenosine triphosphate [1–3]. This injury is accentuated by reperfusion [4–6]. Slow-channel calcium blockers have been shown to offer protection to the ischemic myocardium [7–9]. The effects of calcium antagonist are temperature dependent, with no demonstrable effect at hypothermia [10–12]. Nifedipine is the best studied of the calcium antagonists, and has demonstrated effectiveness in both animals and humans [13–16].

Nicardipine is a new calcium antagonist belonging to the dihydropyridine group. It is structurally related to nifedipine, but has a more specific pharmacologic action than nifedipine. In isolated tissue preparations nicardipine has twice the specificity for vascular tissue compared with papillary muscle than nifedipine [17]. Nicardipine has been shown to have a greater specificity for coronary arteries over mesenteric arteries, whereas nifedipine has an equal affinity for both tissues [18, 19]. Nicardipine has significantly less myocardial depressant effect than nifedipine [20] and has a favorable effect on the myocardial oxygen supply to demand ratio [21].

There are several pharmacologic properties that make nicardipine a more attractive agent for use in cardioplegia than nifedipine. Nicardipine is 100 times more water soluble than nifedipine. Nicardipine is stable in light for more than 24 hours, whereas nifedipine is rapidly inactivated by light [22]. The potency of the two drugs is similar. The present study was designed to evaluate the efficacy of nicardipine in protecting the myocardium during global ischemia at both normothermia and hypothermia.

Material and Methods

The working left heart perfusion apparatus described by Neely and associates [23] was modified and used for this study. Male Sprague-Dawley rats (weight, 350 to 450 g) were given heparin (sodium heparin, 400 units intraperitoneally) and anesthetized with 7.2% chloral hydrate, 0.5 mL/100 g intraperitoneally. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985). Hearts were rapidly excised and placed immediately into Krebs-Henseleit bicarbonate buffer at 2°C. The aorta was cannulated and retrograde perfusion at a pressure of 100 cm H_2O was begun. The perfusate consisted of a modified Krebs-Henseleit bicarbonate

---

Accepted for publication Feb 18, 1992.

Address reprint requests to Dr Clark, Cardiovascular and Pulmonary Research Center, Allegheny General Hospital, 320 E North Ave, Pittsburgh, PA 15212.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

buffer containing 0.4 U insulin/L, 15 mmol/L glucose, and normal rat plasma levels of amino acids:

Na^+	142 mEq/L
K^+	5.8 mEq/L
Cl^-	122 mEq/L
HCO_3^-	25 mEq/L
Ca^{2+}	3.0 mEq/L
Mg^{2+}	2.4 mEq/L
SO_4^-	2.4 mEq/L
$H_2PO_4^-$	1.2 mEq/L
pH	7.4–7.5
Oxygen tension	450–550 mm Hg
Carbon dioxide tension	30–35 mm Hg
Insulin	0.4 U/L
Glucose	15 mmol/L
Aspartic acid	1.86 mg/L
Asparagine	8.99 mg/L
Glutamic acid	17.65 mg/L
Glutamine	95.27 mg/L
Serine	25.96 mg/L
Threonine	24.17 mg/L
Glycine	25.24 mg/L
Alanine	29.05 mg/L
Methionine	8.05 mg/L
Valine	22.03 mg/L
Isoleucine	14.17 mg/L
Leucine	21.77 mg/L
Phenylalanine	11.40 mg/L
Tyrosine	12.50 mg/L
Lysine	69.43 mg/L
Arginine	20.73 mg/L
Proline	12.43 mg/L
Cysteine	7.88 mg/L
Tryptophan	10.21 mg/L
Histidine	44.97 mg/L

The perfusate was kept at 37.5°C and gassed with 95% oxygen and 5% carbon dioxide. The perfusate was filtered through a 0.2-μm Pall cardioplegia filter and not recirculated. During retrograde perfusion, the left atrium was cannulated. After 15 minutes of retrograde perfusion the heart was changed to the working mode. The inflow pressure to the left atrium was 15 cm H_2O. The left ventricle ejected into a compliance chamber with a 2.5-mL air cap, and against a hydrostatic pressure of 80 cm H_2O. The perfusate was recirculated during the working mode, with a 0.2-μm Pall cardioplegia filter in line. After 15 minutes of stabilization, baseline hemodynamic measurements were taken. Aortic flow and coronary flow were measured by timed, volumetric collection of the aortic output and the effluent from the right side of the heart, respectively. Aortic pressure and heart rate were measured from a pressure transducer in line with the aortic cannula. Three measurements were taken for each variable at 5-minute intervals and averaged for the preischemic value. Hearts with rates less than 220 beats/min, aortic flow less than 45 mL/min, or coronary flow greater than 60% of the aortic flow were rejected from the study.

Normothermic Ischemia

Cardiac arrest was achieved with a single 20-mL dose of cardioplegia, which consisted of oxygenated Krebs-Henseleit bicarbonate buffer containing an additional 15 mEq/L of potassium chloride at 37.5°C. The cardioplegia was given at a pressure of 80 cm H_2O and filtered through a 0.2-μm Pall cardioplegia filter. Nicardipine (Cyntex Corp, Palo Alto, CA) was added to the cardioplegia in varying concentrations with the total dose ranging from 2 μg to 6 μg. The control group received cardioplegia without nicardipine. The temperature of the hearts was maintained at 37.5°C throughout the ischemic period of 27 minutes.

Hypothermic Ischemia

Cardiac arrest was achieved with 20 mL of oxygenated National Institutes of Health experimental cardioplegia at 10°C. The composition of the cardioplegia was as follows:

Na^+	90 mEq/L
K^+	23 mEq/L
Cl^-	90 mEq/L
HCO_3^-	30 mEq/L
Ca^{2+}	0.1 mEq/L
Glucose	575 mg/dL
Mannitol	25 g/L
Osmolality	405 mOsm/L
Oxygen tension	750 mm Hg
Carbon dioxide tension	10 mm Hg
pH	7.9–8.1

The cardioplegia was given at a pressure of 80 cm of H_2O and filtered through a 0.2-μm Pall cardioplegia filter. The hearts were rapidly cooled to 10°C and maintained at that temperature throughout the period of ischemia. An additional 20 mL of cardioplegia was given every 30 minutes during the ischemic period. Nicardipine was added to the cardioplegia in varying concentrations with total doses ranging from 1.4 μg to 6.4 μg. The control groups received cardioplegia without nicardipine. The total period of ischemia was 210 minutes or 240 minutes.

After Ischemia

At the end of the ischemic period, the hearts were reperfused for 15 minutes in a retrograde manner as described previously. The hearts were then changed to the working mode. Survival of ischemia was defined as the ability of the heart to generate aortic flow against an afterload of 80 cm H_2O. After 15 minutes of stabilization, the hemodynamic variables of the hearts that survived the ischemic period were measured. Each variable was measured three times at 5-minute intervals, with the average of these three measurements taken for the postischemic value.

Statistics

The hemodynamic results are expressed as percentage of recovery of the preischemic value for each heart. Hemodynamic recovery was calculated using only those hearts that survived the ischemic interval. Significant differences between groups for recovery of function were determined

Table 1. Nicardipine Dosage Groups and Survival of Ischemia

Group	N	No. of Survivors	% Survival	Nicardipine Concentration (μg/mL)	Nicardipine Total Dose (μg)
27 Minutes of Normothermic Ischemia					
A	13	6	46	Control	Control
B	5	3	60	0.10	2
C	8	7	88[a]	0.15	3
D	9	9	100[a]	0.20	4
E	8	6	75	0.25	5
F	8	4	50	0.30	6
210 Minutes of Hypothermic Ischemia					
G	10	10	100	Control	Control
H	7	7	100	0.01	1.4
I	9	8	89	0.02	2.8
J	8	8	100	0.03	4.2
K	7	7	100	0.04	5.6
240 Minutes of Hypothermic Ischemia					
L	10	6	60	Control	Control
M	10	9	90	0.01	1.6
N	10	6	60	0.015	2.4
O	9	7	78	0.02	3.2
P	9	7	78	0.03	4.8
Q	8	7	88	0.04	6.4

[a] $p < 0.05$ compared with control.

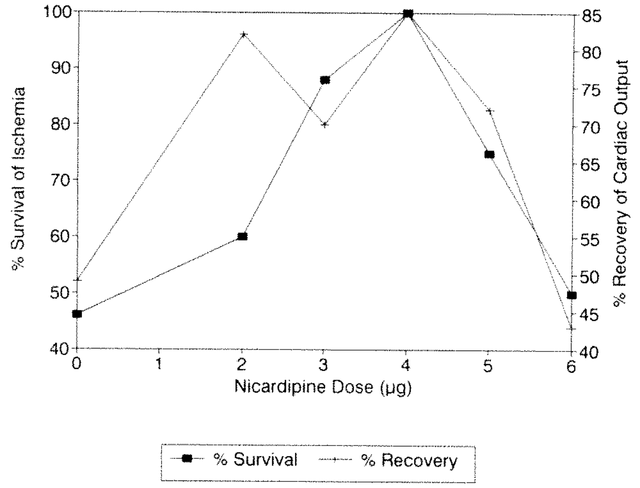


Fig 1. Nicardipine dose-response curve for survival of ischemia and recovery of cardiac output after 27 minutes of ischemia at 37.5°C.

by the Student's *t* test and analysis of variance. The χ^2 and Fisher's exact test were used to determine differences in survival between groups.

Results

Nicardipine provided significant protection to the globally ischemic myocardium at 37.5°C. The control group had 46% survival after 27 minutes of normothermic ischemia, whereas all groups receiving nicardipine had 50% or greater survival of ischemia (Table 1). This reached statistical significance in groups C (88% survival) and D (100% survival) ($p < 0.05$). Postischemic recovery of left ventricular function was also significantly greater in the hearts receiving nicardipine (Table 2). There was a significantly higher percent recovery of aortic flow and cardiac output in groups B and D compared with the control group ($p < 0.05$). Recovery of stroke volume was increased in groups B, D, and E ($p < 0.05$). The optimal dose of nicardipine for myocardial preservation at 37.5°C was 2 to 4 μg (Fig 1). Higher doses of nicardipine did not demonstrate this

Table 2. Hemodynamic Recovery After Ischemia[a]

		Percent Recovery				
Group	N	Aortic Flow	Heart Rate	Coronary Flow	Stroke Volume	Cardiac Output
27 Minutes of Normothermic Ischemia						
A	6	35.1 ± 10.0	102.6 ± 2.8	91.3 ± 5.9	48.2 ± 8.2	49.1 ± 8.3
B	3	75.5 ± 6.3[b]	98.8 ± 4.2	96.7 ± 2.2	83.6 ± 7.6[b]	81.9 ± 4.4[b]
C	7	64.2 ± 9.2	98.2 ± 2.9	87.9 ± 3.2	71.9 ± 7.1	70.2 ± 6.6
D	9	81.1 ± 7.1[c]	97.9 ± 2.3	97.0 ± 3.6	87.3 ± 6.0[c]	85.1 ± 5.9[c]
E	6	59.0 ± 12.0	98.4 ± 3.0	100.7 ± 8.6	73.0 ± 6.3[b]	72.5 ± 7.8
F	4	29.7 ± 9.6	89.0 ± 4.0[b]	80.0 ± 4.5	49.7 ± 9.3	43.3 ± 6.9
210 Minutes of Hypothermic Ischemia						
G	10	82.5 ± 5.2	102.6 ± 5.4	89.4 ± 2.5	84.7 ± 5.4	84.7 ± 3.6
H	7	86.3 ± 7.2	86.4 ± 8.8	96.1 ± 4.6	109.9 ± 11.1	89.4 ± 5.0
I	8	67.8 ± 8.3	93.5 ± 4.9	85.4 ± 4.2	77.6 ± 5.5	73.2 ± 6.6
J	8	81.5 ± 4.9	106.7 ± 3.6	95.4 ± 4.1	80.0 ± 4.3	84.9 ± 3.9
K	7	79.1 ± 12.1	94.4 ± 2.6	101.1 ± 4.9	89.8 ± 8.5	85.5 ± 9.6
240 Minutes of Hypothermic Ischemia						
L	6	72.6 ± 7.2	91.1 ± 5.8	94.6 ± 11.0	88.3 ± 4.6	79.3 ± 2.8
M	9	53.3 ± 13.6	86.2 ± 4.3	81.7 ± 7.3	67.5 ± 10.7	60.1 ± 11.2
N	6	69.8 ± 6.5	94.3 ± 3.6	94.4 ± 6.3	81.4 ± 5.4	76.5 ± 5.1
O	7	86.5 ± 6.4	100.4 ± 7.9	81.7 ± 3.5	86.3 ± 5.3	85.2 ± 4.9
P	7	62.0 ± 5.9	85.6 ± 2.4	100.4 ± 12.8	83.2 ± 7.1	71.0 ± 6.1
Q	7	78.6 ± 9.3	94.8 ± 3.8	96.2 ± 2.6	86.0 ± 5.3	82.4 ± 7.2

[a] Recovery of function calculated using hearts that survived ischemia; values are mean ± standard error of the mean. [b] $p < 0.05$ compared with control. [c] $p < 0.01$ compared with control.

myocardial protective effect. There were no statistically significant differences in the recovery of coronary flow between the control group and the groups treated with nicardipine. Group F had a significantly lower recovery of heart rate compared with the control group ($p < 0.05$).

Nicardipine offered no significant protection to the globally ischemic myocardium when given at 10°C. This study failed to demonstrate significant differences in survival of ischemia (see Table 1) or postischemic recovery of left ventricular function (see Table 2) between the control groups and treated groups when nicardipine was given at 10°C.

Comment

This study with the isolated working rat heart clearly demonstrates that nicardipine offers significant protection to the globally ischemic myocardium at normothermia. Untreated isolated rat hearts suffered significant myocardial injury after 27 minutes of normothermic ischemia. Only 46% of the hearts survived the ischemic period and were able to produce cardiac work after ischemia. The hearts that did survive had a significant decrease in aortic flow, stroke volume, and cardiac output after ischemia. The addition of nicardipine to the cardioplegia provided a significant myocardial protective effect. This protection is evident on the basis of increased survival of ischemia and better hemodynamic recovery after ischemia.

The dose-response curve reveals that the optimal dose of nicardipine is 2 to 4 μg, with a decrease in the effectiveness of the drug at higher or lower doses. Similar bell-shaped dose-response curves have been demonstrated with other calcium antagonists [10, 11, 24]. The reason for this decrease in myocardial protective properties at higher doses is not clear, but several theories have been proposed. At high doses some of the drug may remain bound to the cell membrane after reperfusion. This residual drug may exert a myocardial depressant effect and suppress the functional recovery of the myocardium after ischemia. At high doses nicardipine may permanently alter the cell membrane and the flux of calcium ions. This permanent change in the function of the cell membrane may result in a decrease in functional recovery after ischemia.

We were able to demonstrate no benefit to the ischemic myocardium from the administration of nicardipine at 10°C. Other calcium antagonists have been shown to lose their myocardial protective effects under hypothermic conditions [10–12]. One possible explanation for this finding is that hypothermia and calcium antagonists may provide myocardial protection through a common mechanism. This would result in no additional improvement in functional recovery after ischemia if hypothermia and calcium antagonists are used simultaneously. Nifedipine has been shown, however, to have myocardial protective effects during hypothermia if the heart is pretreated with the drug before the initiation of hypothermic ischemia [25]. This argues against the common mechanism hypothesis. Another possible explanation is that the drug does not bind with the cell membrane under hypothermic conditions and is not able to exert its myocardial protective effects. Hypothermia may effect a phase transition in the lipoprotein of the cell membrane, resulting in an alteration of the three-dimensional structure of the receptor. This could prevent the drug from binding to the receptor. The inability of the drug to bind to the receptor on the cell membrane results in a lack of myocardial protective effects. Further experiments are required to determine the mechanism of action of the myocardial protective effects of nicardipine and the reason for the loss of this activity at hypothermia.

In conclusion, nicardipine provides significant myocardial protection to the isolated rat heart during normothermic ischemia. This study demonstrates that the dose-response curve for this myocardial protective effect is bell-shaped, with an optimum dose of 2 to 4 μg. The myocardial protective effect of nicardipine is lost when the drug is given under hypothermic conditions. Further studies are required to determine if pretreatment with nicardipine before the initiation of hypothermia will result in improved myocardial preservation during hypothermic ischemia.

We thank Gerald D. Kelly and David M. Flynn for their assistance in the isolated heart laboratory, and Mary Manasco for preparation of the manuscript.

References

1. Katz AM, Reuter H. Cellular calcium and cardiac cell death. Am J Cardiol 1979;44:188–90.
2. Henry PD, Shuchleib R, Davis J, Weiss ES, Sobel BE. Myocardial contracture and accumulation of mitochondrial calcium in ischemic rabbit heart. Am J Physiol 1977;233: H677–84.
3. Shen AC, Jennings RB. Myocardial calcium and magnesium in acute ischemic injury. Am J Pathol 1972;67:417–40.
4. Shen AC, Jennings RB. Kinetics of calcium accumulation and acute myocardial ischemic injury. Am J Pathol 1972;67: 441–52.
5. Bers DM, Langer GA. Uncoupling cation effects on cardiac contractility and sarcolemmal Ca^{2+} binding. Am J Physiol 1979;237:H332–41.
6. Watts JA, Koch CD, LaNone KF. Effects of Ca^{2+} antagonism on energy metabolism: Ca^{2+} and heart function after ischemia. Am J Physiol 1980;238:H909–16.
7. McGoon DC. The ongoing quest for ideal myocardial protection. J Thorac Cardiovasc Surg 1985;89:639–53.
8. Balderman SC, Chan AK, Cage AA. Verapamil cardioplegia: improved myocardial preservation during global ischemia. J Thorac Cardiovasc Surg 1984;88:57–66.
9. Vouhé PR, Hélias J, Grondin CM. Myocardial protection through cold cardioplegia using diltiazem, a calcium channel blocker. Ann Thorac Surg 1980;30:342–8.
10. Yamamoto F, Manning AS, Braimbridge MV, Hearse DJ. Cardioplegia and slow calcium-channel blockers. J Thorac Cardiovasc Surg 1983;86:252–61.
11. Yamamoto F, Manning AS, Braimbridge MV, Hearse DJ. Calcium antagonist and myocardial protection: diltiazem during cardioplegic arrest. Thorac Cardiovasc Surg 1983;31: 369–73.
12. Hearse DJ, Yamamoto F, Fukunami M, Baker JE, Shattock MJ. The apparent temperature-dependency of calcium antagonist. Circulation 1983;68(Suppl 3):184.
13. Clark RE, Christlieb IY, Ferguson TB, et al. The first American clinical trial of nifedipine in cardioplegia. J Thorac Cardiovasc Surg 1981;82:848–59.

14. Clark RE, Christlieb IY, Ferguson TB, et al. Laboratory and initial clinical studies of nifedipine, a calcium antagonist for improved myocardial preservation. Ann Surg 1981;193: 719–32.
15. Boe SL, Dixon CM, Sakert TA, Magovern GJ. The control of myocardial Ca^{2+} sequestration with nifedipine cardioplegia. J Thorac Cardiovasc Surg 1982;84:678–84.
16. Clark RE, Magovern GJ, Christlieb IY, Boe SL. Nifedipine cardioplegia experience: results of a 3-year cooperative clinical study. Ann Thorac Surg 1983;36:654–63.
17. Clarke B, Grant D, Patmore L, Whitting RL. Comparative calcium entry blocking properties of nicardipine, nifedipine and PY 108068 on cardiac and vascular smooth muscle [Abstract]. Br J Pharmacol 1983;79:333P.
18. Clarke B, Eglen RM, Patmore L, Whitting RL. Cardioselective calcium entry blocking properties of a nicardipine metabolite [Abstract]. Br J Pharmacol 1984;83:437P.
19. Takenaka T, Asano M, Shiono K, Shibasaki M, Inagaki O. Cardiovascular pharmacology of nicardipine in animals. Br J Clin Pharmacol 1985;20:7S–22S.
20. Rousseau MF, Pouleur H. Calcium antagonism free of negative inotropic effects? A comparison of intracoronary nifedipine and nicardipine. Circulation 1984;70(Suppl 2):304.
21. Pepine CJ, Lambert CR. Usefulness of nicardipine for angina pectoris. Am J Cardiol 1987;59:13J–9J.
22. Bottorff MB, Graves DA, McAllister RG, Batenhorst RL, Foster TS. Nifedipine stability in cardioplegic solution. Am J Hosp Pharm 1984;41:2068–70.
23. Neely JR, Liebermeister H, Battersby EJ, Morgan HE. Effect of pressure development on oxygen consumption by isolated rat heart. Am J Physiol 1967;212:804–14.
24. Nayler WG, Grau A, Slade A. A protective effect of verapamil on hypoxic heart muscle. Cardiovasc Res 1976;10:650–62.
25. Nayler WG. Protection of the myocardium against postischemic reperfusion damage. J Thorac Cardiovasc Surg 1982;84: 897–905.

Electrophysiologic Study of Dysrhythmias After Atrial Operations in Dogs

Tatsuo Tamiya, MD, Toshiyuki Yamashiro, MD, Atsushi Hata, MD, Kenshi Kuge, MD, Sohichi Asano, MD, and Takayuki Sato, MD

Second Department of Surgery and First Department of Physiology, Kochi Medical School, Kochi, Japan

Experiments were conducted with 159 dogs to investigate the mechanism of persistent dysrhythmias clinically encountered after atrial-level operations. Those found after incisions to the internodal pathways (INPs) of the right atrium were analyzed using cardiac mapping in an anesthetized or extracorporeally perfused state. Longitudinal incisions of the posterior INP often allowed inducible sustained atrial flutter, with circus movement of excitation around the right atrium near the tricuspid orifice. Sustained atrial flutter thus produced was modified in cycle length by coexisting division of the middle INP but inhibited by that of the anterior INP. Its incidence increased at chronic stage, with marked cicatricial changes. The disrupted anterior INP markedly prolonged conduction time to the atrioventricular node and A-H interval compared with the other disruptions. Persistent atrioventricular junctional rhythm developed in about 50% of the animals after disruption of all three INPs or anterior and posterior INPs; division of the anterior INP was the common potent factor, although no single blocked INP produced persistent junctional rhythm. Our results support the "summation theory." The incidence of junctional rhythm and hypoxia of the sinoatrial node (flow rate of less than 10 mL · 100 g^{-1} · min^{-1}) were markedly enhanced by coexisting blockade of atrial feeding arteries in addition to division of the anterior INP. In conclusion, massive posterior INP disruption is a potent anatomic substrate in producing sustained atrial flutter, middle INP division a modifier, and anterior INP division an inhibitor. Division of the anterior INP is a potent anatomic substrate in producing junctional rhythm, and hypoxia involving the sinoatrial node reacts as its synergic factor.

(Ann Thorac Surg 1992;54:717–24)

Persistent dysrhythmias produced by surgical intervention in the atrium can be lethal in the postoperative period [1–10]. The mechanism, however, has not been thoroughly clarified. In 1967 and 1968, we experienced six unexpected disasters in 11 patients undergoing closure of atrial septal defect through an incision along the crista terminalis (CT) [4]. Six of the patients showed miscellaneous persistent supraventricular dysrhythmias, and 1 died suddenly 2½ years after operation. No cause for dysrhythmia was found in histologic studies of the right atrium, pulmonary arterial pressure, or age, except for large defects often with poorly formed lower margin. Dysrhythmias were not prevented by deviating the incision far from the sinoatrial (SA) node area. However, these dysrhythmias have not developed since abandoning the incision along the CT.

Similar dysrhythmias have been reported after atrial baffling procedures for transposition of the great arteries [5–10]. Experiments to determine the mechanisms of these dysrhythmias to date have been done mainly on isolated perfused hearts [11–13]. We performed experiments in an anesthetized canine model to evaluate these dysrhythmias under near-physiologic conditions. We observed atrial flutter (AF) and supraventricular bradyarrhythmias intraoperatively or postoperatively and were able to correlate them to the location of the incision.

Material and Methods

Subjects

One hundred fifty-nine mongrel dogs of both sexes weighing 9 to 17 kg were given incisions to the right atrial (RA) free wall, incisions to the interatrial septum in relation to the internodal pathway (INP) [14], and/or blockade of the RA feeding arteries (Fig 1). Any dog in which arrhythmia developed before these incisions was removed from the experimental group.

The dogs were anesthetized with pentobarbital (30 mg/kg intravenously) and ventilated with a Harvard respirator. The chest was opened in the fourth right intercostal space, and the pericardium was incised to provide free access to the venae cavae and right atrium. The tissue on the incision line was clamped, incised, and closed with a running suture (5-0 Prolene; Ethicon, Somerville, NJ). A wide margin of tissue on each side of the longitudinal and transverse incisions of the INPs was sewn in to involve the INPs. The SA node was always avoided.

Traumatization of the Right Atrium

The dogs were divided into four groups. Group A consisted of 100 dogs given one of ten different incisions in the RA free wall. Table 1 (group A) and Figure 1A summarize the details and frequency of each incision. Group A was mainly used for analysis of AF. Maps were made at both acute and chronic stages, with an interval of 84 to 105 days, in 8 dogs subjected to RA free wall incision

---

Accepted for publication Feb 19, 1992.

Address reprint requests to Dr Tamiya, Second Department of Surgery, Kochi Medical School, Nankoku, Kochi, Japan 783.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

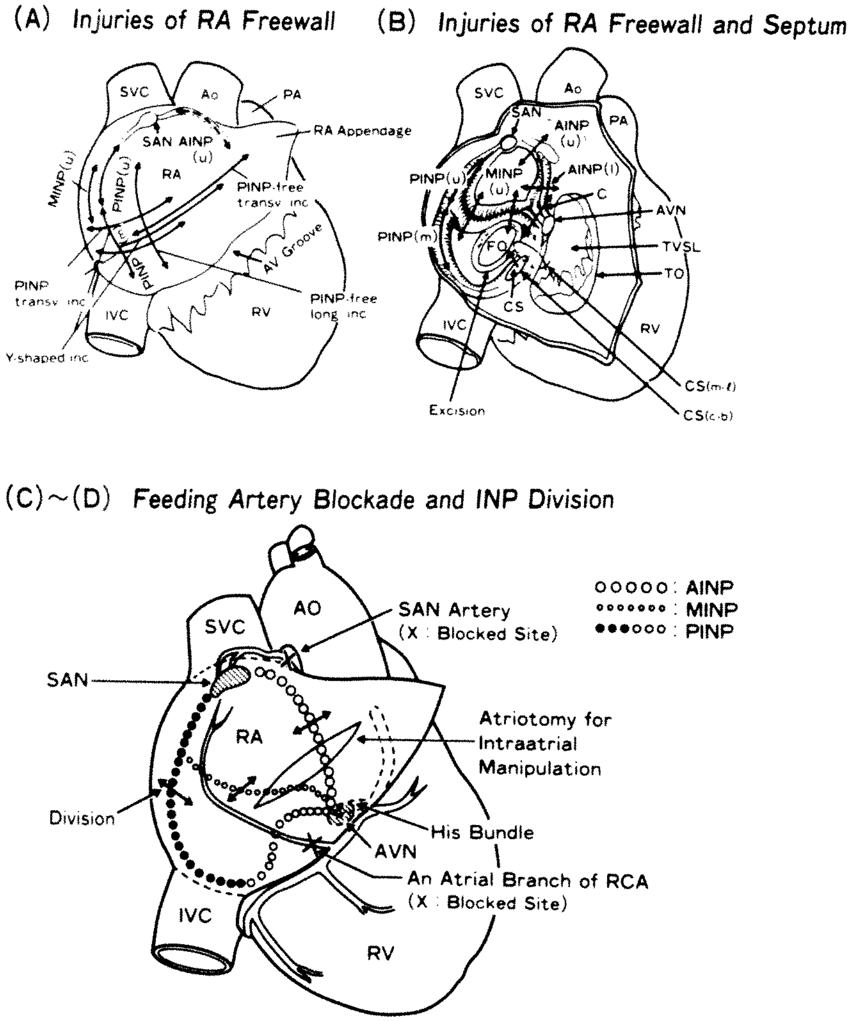


Fig 1. Various incisions and feeding artery blockade in the right atrium. (AINP = anterior INP; Ao = aorta; AV = atrioventricular; AVN = atrioventricular node; C = portion where INPs converge (arbitrary assignment); CS = coronary sinus; CS(c-b) = cutback of coronary sinus; CS(m-l) = mass ligation of coronary sinus; CT = crista terminalis; FO = fossa ovalis; INP = internodal pathway; IVC = inferior vena cava; l = lower incised portion of INP; long. inc. *= longitudinal incision; m = middle incised portion of INP; MINP = middle INP; PA = pulmonary artery; PINP = posterior INP; RA = right atrial; RCA = right coronary artery; RV = right ventricle; SAN = sinoatrial node; SVC = superior vena cava; TO = tricuspid orifice;* trans. inc. *= transverse incision; TVSL = tricuspid valve septal leaflet; u = upper incised portion of INP.)*

Table 1. Assignment of Dogs for Incisions

Group	No. of Dogs
A (free wall incisions)	
PINP-free longitudinal incision	20
PINP longitudinal incision	20
Y-shaped incision	8
PINP-free transverse incision	8
PINP-across transverse incision (single)	8
PINP-across transverse incision (double)	8
AINP longitudinal incision	7
AINP + PINP incision	7
MINP transverse incision	7
MINP + PINP incision	7
Subtotal	100
B (free wall + septum incision)	
Non-CPB subgroup	7
CPB subgroup	31
Subtotal	38
C (feeding artery blockade)	6
D (feeding artery blockade + INP division)	15
Grand total	159

AINP = anterior INP; CPB = cardiopulmonary bypass; INP = internodal pathway; MINP = middle INP; PINP = posterior INP.

involving posterior INP (PINP) disruption and in 8 dogs subjected to free wall incision without involving the PINP. After chronic electrophysiologic study, the atrial specimens were examined by a 10-μm section technique followed by staining with hematoxylin and eosin.

In group B, two approaches were employed for traumatization of the interatrial septum in 38 dogs (see Table 1, group B). One was a quick incision and suturing of the proposed portion of the INP through an atriotomy parallel to the atrioventricular (AV) groove apart from the CT, while the right atrial cavity was kept relatively blood-free by transient occlusion of both venae cavae (7 dogs). The other was the careful incision and suturing of the proposed portion through an atriotomy under nonblood-primed total cardiopulmonary bypass (CPB) with a bubble oxygenator (BOS 5; temperature, 36° ± 0.5°C; 31 dogs). Traumatization of the interatrial septum and RA free wall INP was done through one of seven incisions illustrated in Figure 1B.

In group C, feeding arteries to the RA were blocked by either ligation or division, without injury to the INPs, under CPB in 6 dogs, as shown in Figures 1C and 1D. An atrial branch of the right coronary artery, ascending along the CT after crossing the frontal RA free wall, was considered an important canine atrial feeder, besides the

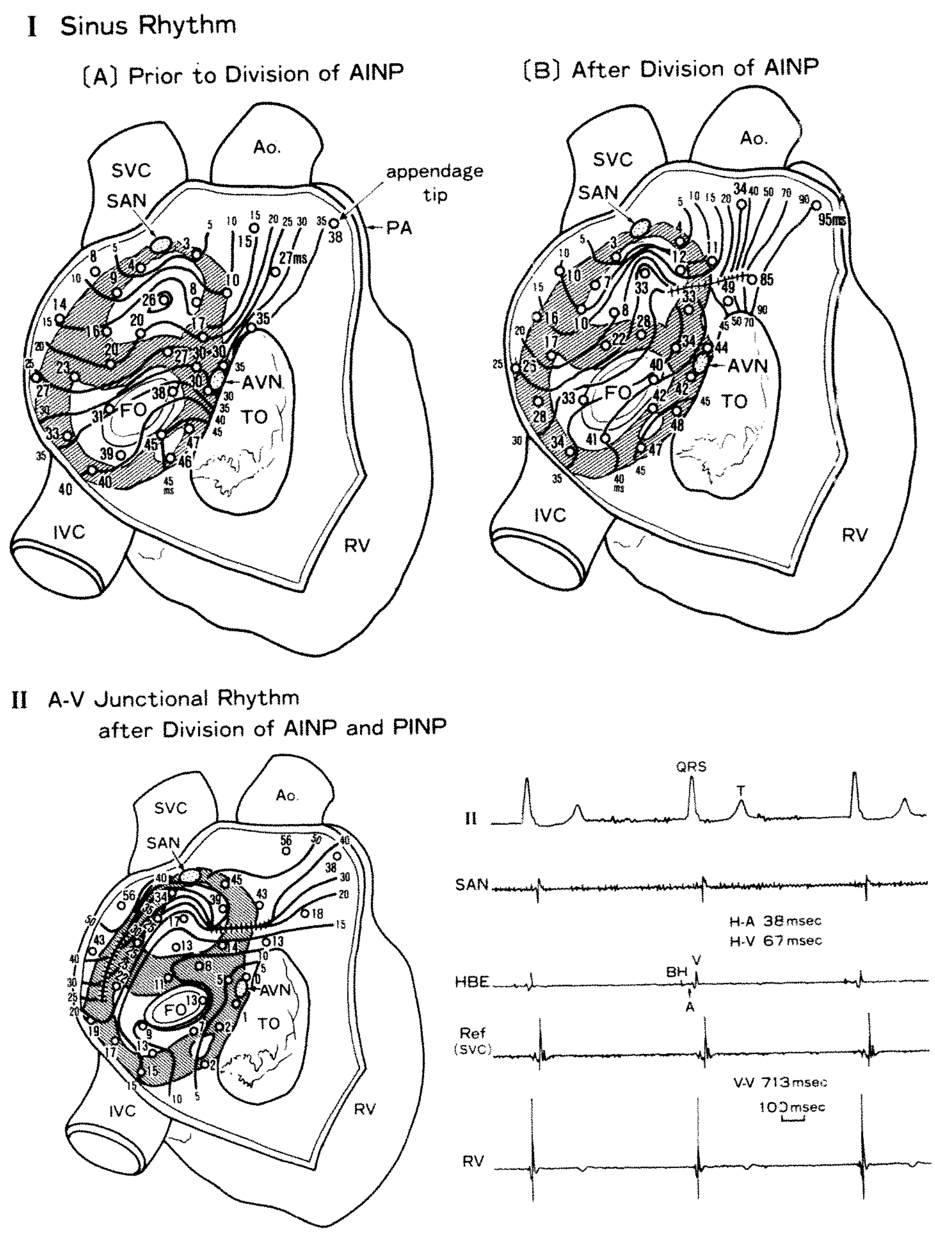


Fig 2. Endocardial propagation of excitation. Thirty points were mapped for right atrium endocardial recording under cardiopulmonary bypass. Sinus rhythm is shown in (I) and junctional rhythm in (II). Number by each open circle indicates the conduction time (ms) from the earliest excitation point of the right atrium. (HBE = His bundle electrocardiogram; Ref = referential electrode on the SVC close to the SAN; other abbreviations are as in Figure 1.)

so-called SA node artery, which has generally been accepted [8]. Regional blood flow such as that in the SA node area was measured to evaluate the influence of hypoxia on occurrence of junctional rhythm (JR).

In group D, the RA feeding arteries were blocked, with division (ie, transection) of the INPs under CPB, in 15 dogs as presented in Figures 1C and 1D. The divided portions were not sewn in this group purposely. The regional blood flow was measured to evaluate the influence of both hypoxia and INP incision on occurrence of JR. Cardiopulmonary bypass in groups C and D was done identically to that in group B.

Instrumentation for Electrical Stimulation, Cardiac Mapping, and Tissue Blood Flow Determination

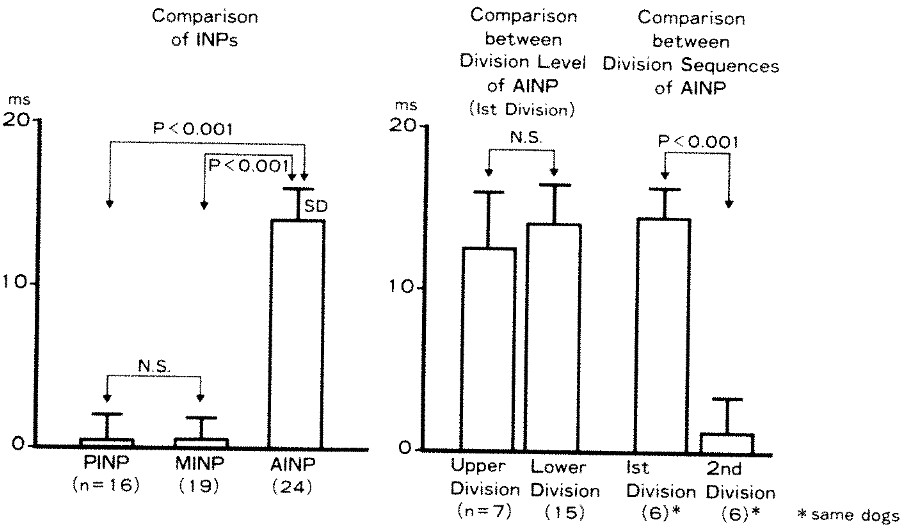
A Medtronic model 5325 programmable stimulator (Medtronic, Minneapolis, MN) was used to initiate atrial dysrhythmias intraoperatively. The atrium was paced through an electrode at a cycle length of 75 ms for 30 seconds.

An HPM-7100 mapping system (Fukuda Denshi Co Ltd, Tokyo, Japan) was used for both epicardial and endocardial mappings. One rectangular array (49.5 × 30 mm) with 24-point bipolar electrodes set 7.5 mm apart was used (bipolar electrode distance of 1 mm). An Electro-Catheter model 89-1097 endocardial electrode (Elecath, Rahway, NJ) was used, and the referential lead was placed on the SA node. Both epicardial and endocardial maps were recorded on paper and floppy disc.

A Siemens-Elema Mingograf 82 (Siemens-Elema AB, Solna, Sweden) was also used for optional purposes (0.003 second time constant, 550 Hz high-cut filter, and 100 mm/s paper speed). For example, 30 points on the RA endocardium were mapped for recording as shown in Figure 2.

Mapping was done during normal sinus rhythm, AF,

Fig 3. Delay of conduction to the AV node due to disruption of INPs in CPB subgroup of group B (free wall + septum incision). (Note: "CS cut-back alone" is excluded in the dogs with PINP incisions.) (N.S. = *not significant;* SD = *standard deviation; other abbreviations are as in Figure 1.)*



and JR, without pacing in principle. A-A, A-H, and H-V intervals and corrected sinus node recovery time were determined by the Mingograf. Activation time was determined on the criteria established by Funada and associates [15]. Definition of JR and AV dissociation was based on the criteria given by Narula [16].

Regional tissue blood flow was determined by laser flowmeter model ALF 21 (Advance Co Ltd, Tokyo, Japan) and its type C probes. The 10 mm in diameter round flat tip of the probe was directly attached to any portion of interest, such as the SA node area, by means of Aron-Alpha glue.

Statistical Analysis

A *t* test was used for statistical analysis, except for the incidence of JR in Table 2, where a χ^2 test was employed.

Results

Changes in Propagation of Excitation in the Right Atrium

GROUP A. Before incision, excitation originating from the SA node spread over the RA free wall in a radial fashion (fastest along the CT). The conduction time from the SA node to breakthrough of the right ventricle before incision was 125.0 ± 31.7 ms (mean ± standard deviation; n = 100). After incision, the propagation pattern of excitation over the RA free wall was specific to each traumatization. Longitudinal incision along the CT brought a marked conduction delay of 20 to 40 ms in an extensive portion of the free wall, involving not only the CT but also its neighboring structures such as the pectinate muscles. The Y-shaped incision produced an additional delay in the transverse incision. The longitudinal incision anterior to the CT brought a delay in a portion caudal or anterior to the incision, but did not in either the CT or structures posterior to the trauma. Compared with the single transverse incision, the double transverse incisions resulted in a further delay to the portion caudal to the lower incision. Trauma along the arch of the crista [11] had little influence on propagation over the anterior atrial free wall.

GROUP B. Conduction time from the SA node to the AV node (to the upper half of Koch's triangle) was measured in dogs under CPB (n = 28; 3 dogs with ectopic rhythm before disruption were omitted). It was 30.71 ± 1.91 ms before disruption of the INP (Fig 3).

There was little prolongation by division of either the upper or lower portions of the PINP (0.53 ± 1.23 ms; n = 19) or division of upper or lower portions of the middle INP (MINP) (0.50 ± 1.41 ms; n = 16). There was marked prolongation, however, by division of the upper or lower anterior INP (AINP) (14.58 ± 3.01 ms; n = 24). No significant difference was found in the delay between the upper and lower transections of the AINP (12.86 ± 3.27 ms [n = 7] versus 14.33 ± 2.47 ms [n = 15], respectively). However, far greater delay occurred when the AINP was initially transected than when subsequently done, regardless of the transected level ($p < 0.001$). In all dogs subjected to disruption of INP, endocardial maps demonstrated circumventing conduction to the AV node (n = 28) unless ectopic excitation participated in the event (n = 3). The pattern was specific to the trauma (see Fig 2).

Of the initial transection of the INP, disruption of the AINP prolonged the A-H interval 8.33 ± 5.82 ms (n = 6), that of the MINP prolonged it 2.00 ± 1.41 ms (n = 4); but that of the PINP shortened it 5.20 ± 4.12 ms (n = 5). The interval in the former was significantly longer than that in either of the latter two ($p < 0.05$).

Atrial Flutter

The dogs in group A were rapidly paced (800 beats/min) acutely to determine the incidence of sustained AF in each of the incision groups. (Sustained AF was arbitrarily defined as lasting longer than 5 minutes.) The results are summarized in Figure 4A. Sustained AF was frequently induced in those with PINP disruption, but not in those with PINP-free disruption. The inducibility appeared to be somewhat proportional to the mass of the PINP lesion. Sustained AF induced by PINP disruption was reduced by additional MINP disruption, whereas it was no further induced by AINP disruption.

In Figure 4B, the inducibility of sustained AF is com-

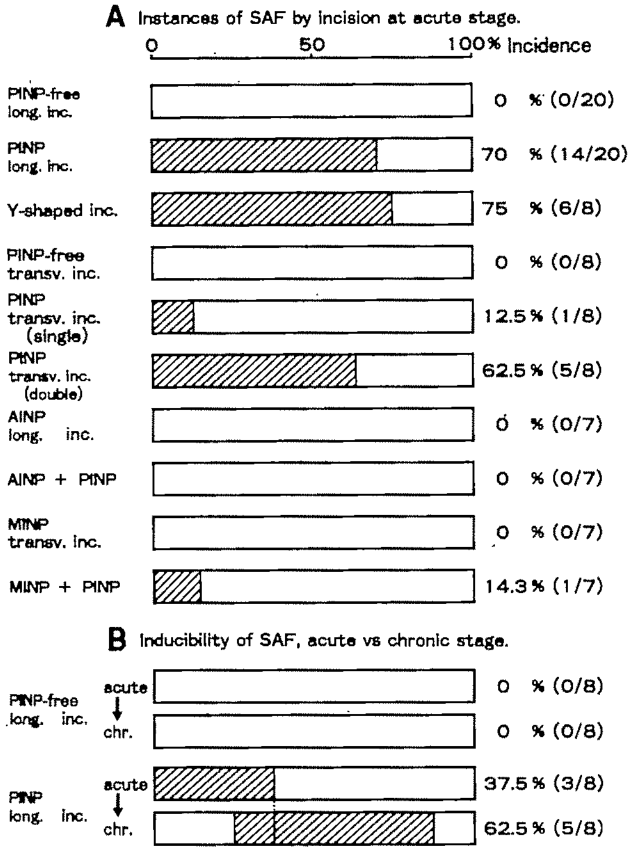


Fig 4. Incidence and inducibility of sustained atrial flutter (SAF) in group A (free wall incisions). (Abbreviations are as in Figure 1.)

pared between acute and chronic stages. It was higher at the chronic stage than at the acute stage in those with PINP disruption, whereas it remained at zero at both stages in those with PINP-free disruption. In dogs with inducible sustained AF in the chronic stage, tissue studies showed marked fibrotic changes over the traumatized site, together with foreign body reactions such as giant cell infiltration around the suture material.

Figure 5 shows the electrophysiologic analysis for dogs with trauma to the INPs—2 in group A and 10 in group B, including 7 on CPB. Of the 12 dogs with longitudinal PINP disruption, sustained AF was produced in 5 with a clockwise activation sequence and 11 with a counterclockwise activation sequence. Figure 6 illustrates the epicardial electrocardiograms taken around the right atrium near the tricuspid orifice of dog 107 during sustained AF; both clockwise and counterclockwise activation sequences were recorded. The relationship between sustained AF and coexisting disruption of the INP was only determined in the 7 dogs with CPB in which precise data were obtained. Four of the dogs showed both clockwise and counterclockwise activation sequences. The cycle length was 118.3 ± 15.9 ms for the clockwise activation sequence and 117.5 ± 9.1 ms for the counterclockwise activation sequence. The frequency of sustained AF produced by PINP disruption was reduced by coexisting MINP division in 2 dogs, but increased in 1 dog. Sustained AF was never induced after AINP division was added.

Supraventricular Bradyarrhythmias

Incidences of supraventricular bradyarrhythmias, such as sinus bradycardia, atrioventricular dissociation, or JR, were not noted in group A; however, such arrhythmias did occur in groups B, C, and D. Table 2 shows the incidence of JR developing in the CPB subgroup of group B. The incidence in the non-CPB subgroup was omitted because accurate information was not always obtained in regard to both septal disruption and measurements. Persistent JR was observed in 9 of 16 dogs with three disrupted INPs and in 4 of 8 with disrupted AINP and PINP; however, it was not observed in any dogs with either disrupted AINP and MINP or disrupted MINP and PINP, or in dogs with any single INP disrupted. Of the 7 dogs in which portion C division was added, 5 had immediate development of JR (both with and without CPB).

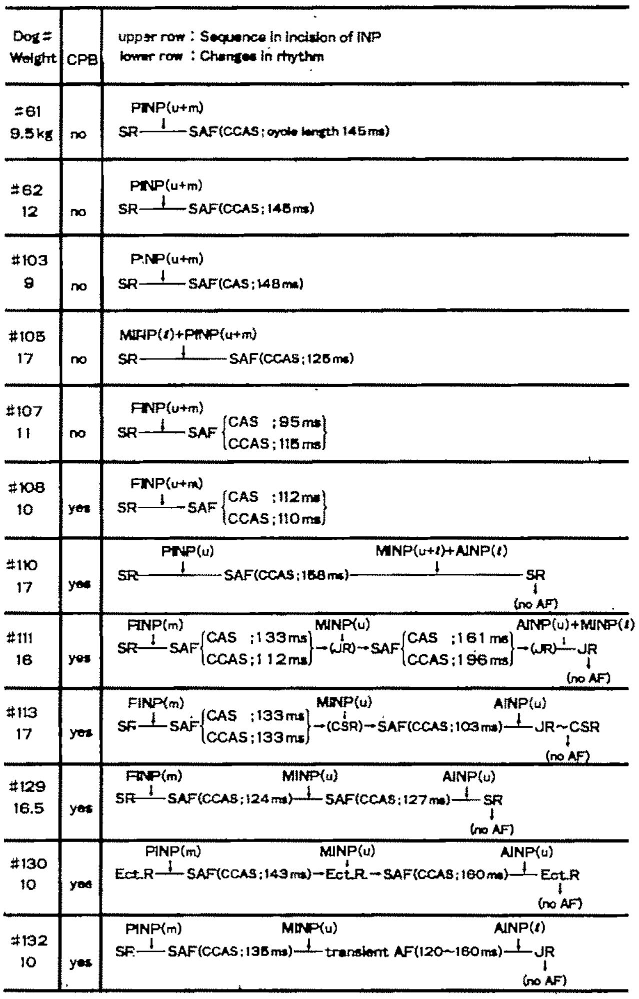

Dog # Weight
CPB
upper row : Sequence in incision of INP
lower row : Changes in rhythm
#61 9.5 kg
no
PINP(u+m)
SR — SAF(CCAS; cycle length 145 ms)
#62 12
no
PINP(u+m)
SR — SAF(CCAS; 145 ms)
#103 9
no
PINP(u+m)
SR — SAF(CAS; 148 ms)
#105 17
no
MINP(ℓ)+PINP(u+m)
SR — SAF(CCAS; 125 ms)
#107 11
no
PINP(u+m)
SR — SAF {CAS ; 95 ms / CCAS; 115 ms}
#108 10
yes
PINP(u+m)
SR — SAF {CAS ; 112 ms / CCAS; 110 ms}
#110 17
yes
PINP(u)
MINP(u+ℓ)+AINP(ℓ)
SR — SAF(CCAS; 158 ms) — SR
(no AF)
#111 16
yes
PINP(m)
MINP(u)
AINP(u)+MINP(ℓ)
SR — SAF {CAS ; 133 ms / CCAS; 112 ms} → (JR) → SAF {CAS ; 161 ms / CCAS; 196 ms} → (JR) — JR
(no AF)
#113 17
yes
PINP(m)
MINP(u)
AINP(u)
SR — SAF {CAS ; 133 ms / CCAS; 133 ms} → (CSR) → SAF(CCAS; 103 ms) — JR ~ CSR
(no AF)
#129 16.5
yes
PINP(m)
MINP(u)
AINP(u)
SR — SAF(CCAS; 124 ms) — SAF(CCAS; 127 ms) — SR
(no AF)
#130 10
yes
PINP(m)
MINP(u)
AINP(u)
Ect.R — SAF(CCAS; 143 ms) → Ect.R → SAF(CCAS; 160 ms) — Ect.R
(no AF)
#132 10
yes
PINP(m)
MINP(u)
AINP(ℓ)
SR — SAF(CCAS; 135 ms) — transient AF(120~160 ms) — JR
(no AF)

Fig 5. Electrophysiological analysis of sustained atrial flutter (SAF) in 12 dogs induced by rapid pacing in regard to activation sequence, cycle length, and interaction of disrupted INPs. (CAS = clockwise activation sequence; CCAS = counterclockwise activation sequence; CPB = cardiopulmonary bypass; CSR = coronary sinus rhythm; Ect. R = ectopic rhythm; JR = atrioventricular junctional rhythm; SR = sinus rhythm; other abbreviations are as in Figure 1.)

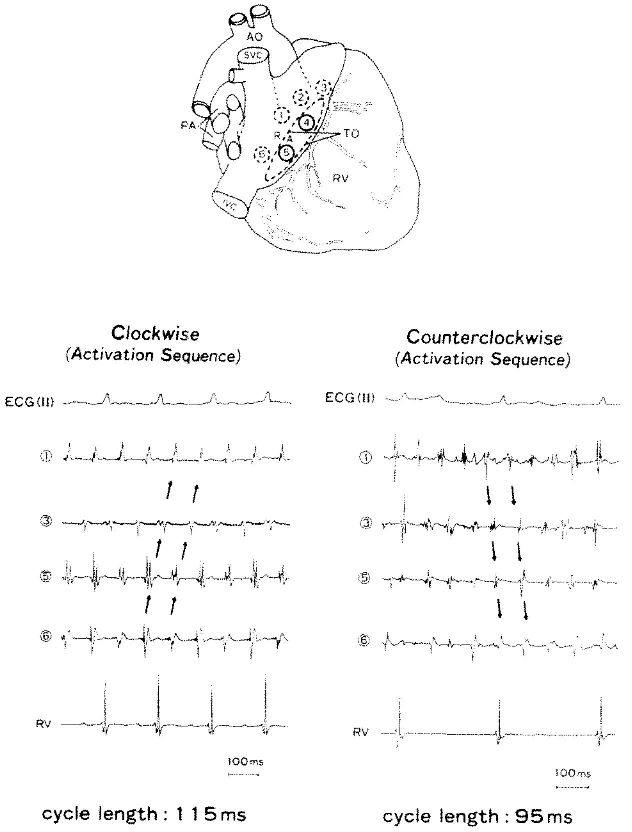


Fig 6. Epicardial electrocardiograms (ECG) simultaneously recorded around right atrium near tricuspid orifice during sustained atrial flutter in dog 107 with disrupted PINP. (Note: The position of the epicardial electrodes is identical to that described by Frame and associates [21]. Point 1 corresponds to the atrioventricular node, and point 6 to the coronary sinus site.) (Abbreviations are as in Figure 1.)

Of the 6 dogs in group C (feeding artery blockade), JR developed in only 1, which had a final flow rate of the SA node area of 8.2 mL · 100 g^{-1} · min^{-1}. The other 5 maintained sinus rhythm with a flow rate of 22.7 ± 8.3 mL · 100 g^{-1} · min^{-1}. The final flow rate in the latter is the value when sinus rhythm persisted after blockade. The control flow rate, which was measured immediately after atriotomy jeopardizing neither the feeding arteries nor the INP, was 39.8 ± 11.0 mL · 100 g^{-1} · min^{-1} (n = 13).

Table 2. Incidence of Atrioventricular Junctional Rhythm Due to Disruption of the Internodal Pathway in the Cardiopulmonary Bypass Subgroup of Group B (n = 26)[a]

Incision	No. of Dogs	Persistent JR[b]	Transient JR	No JR
AINP + MINP + PINP	16	9	1	6
AINP + PINP	8	4	1	3
AINP + MINP	9	0	2	7
PINP + MINP	9	0	1	8
AINP	11	0	1	10
PINP	8	0	0	7
MINP	8	0	0	8

[a] Dogs with coronary sinus cutback alone (2), preoperative ectopic rhythm (1), sinoatrial node injury suspected (1), and coronary sinus division (1) were omitted. [b] Persistent junctional rhythm was arbitrarily defined as lasting longer than 30 minutes.

JR = junctional rhythm; all other abbreviations are as in Table 1.

Table 3. Incidence of Junctional Rhythm and Final Flow Rate in Group D

Subgroup	Incidence/ No. of Dogs	Flow Rate (mL · 100 g^{-1} · min^{-1})
Artery blockade + AINP division	2/2	7.3 ± 0.3
Artery blockade + MINP division	0/3	16.1 ± 5.2
Artery blockade + PINP division	0/2	19.3 ± 2.8
Artery blockade + MINP & AINP division	2/2	5.9 ± 2.8
Artery blockade + PINP & AINP division	2/2	9.4 ± 0.4
Artery blockade + MINP, AINP, & PINP division	4/4	11.1 ± 2.1

Abbreviations are as in Table 1.

Of the 15 dogs in group D (both feeder blockade and INP division), 10 had development of JR with a final flow rate of 8.8 ± 2.9 mL · 100 g^{-1} · min^{-1}, and the other 5 kept sinus rhythm with a flow rate of 17.3 ± 4.6 mL · 100 g^{-1} · min^{-1}. Details of the incidence of JR and final flow rate are shown in Table 3.

All dogs in which JR developed in group D were those subjected to AINP division. All dogs with JR in groups C and D showed mean final flow rates of the SA node area less than 10 mL · 100 g^{-1} · min^{-1} with the exception of the group D subgroup that had all three INPs divided (11.1 mL · 100 g^{-1} · min^{-1}). These rates were much lower than those where sinus rhythm was maintained. The corrected sinus node recovery time was often significantly prolonged ($p < 0.05$) shortly before onset of JR in those subjected to either AINP division or feeding artery blockade.

Comment

In 1920, Lewis and associates [17] suggested the "reentrant hypothesis" to explain AF. Since then a steady flow of evidence supporting their idea that AF results from circus movement around naturally occurring orifices in the atria have been reported. Rosenblueth and Garcia-Ramos [18] induced a somewhat stable AF after crushing the tissues between the venae cavae in dogs (intercaval lesion). They and other investigators [19, 20] suggested that tachycardia was due to reentrant excitation around the barrier consisting of the intercaval lesion and orifices of both venae cavae. Frame and co-workers [21] reported a model of stable inducible AF in dogs in 1986. They added a second incision extending the base of the atrial appendage in connection with the intercaval lesion (Y-shaped lesion). The second incision transected the PINP. They theorized that the greater stability of tachycardia after the Y-shaped incision may be related to the longer tachycardia cycle length, which in turn results in formation of a longer excitable gap. When the impulse follows a longer excitable gap, it propagates through more completely depolarized tissues and therefore has a higher stability. By means of egg-shaped multielectrode arrays inserted into the atria, they made endocardial maps during AF of isolated perfused canine hearts with the Y-shaped lesion and were able to demonstrate that the impulse traveled through the interatrial septum near the tricuspid orifice rather than over the left atrial free wall [12, 21].

A common feature of the atriotomy in our experiment presented here and that of Frame and co-workers [21] was the extensive disruption of the PINP. Both studies observed circus movement of excitation around the right atrium near the tricuspid ring. In the current hypothesis, prerequisites for induction of spontaneous or artificial AF are (1) anatomic or geometric substrate, (2) functional substrate, and (3) trigger [22]. The principal substrate is anatomic abnormality in atrial myocardium, which, when combined with the natural obstacle, creates a discontinuity in conduction, together shaping the potential reentrant pathology. The dimensions of this discontinuity are critical in determining the length of the surrounding pathway and the potential for sustained and stable reentry. The functional substrate is a nonuniform duration of depolarization of myocardium within or adjacent to the potential reentrant pathway. The triggering event is represented by atrial premature depolarization.

In this canine study, the principal anatomic substrate is the specific atriotomy combined with the tricuspid orifice. However, our mapping study suggests that circus movement may involve a somewhat wider zone above the tricuspid orifice with lesser uniformity than that created by Frame and co-workers [21]. In fact, the cycle length of excitation did fluctuate during the onset of sustained AF. In 14 dogs subjected to longitudinal incision of the PINP without CPB, cycle length was 136.14 ± 13.10 ms (variance, 36.1 ± 16.99 ms). This observation does not rule out the likelihood of variety in the circus movement route of AF. This might be derived from our atriotomy, which was more remote from the tricuspid ring than Frame and co-workers', possibly allowing an enhanced dominance of functional substrate and attenuation of the anatomic substrate. A counterclockwise activation sequence was more frequently seen than a clockwise activation sequence, as found by other investigators [12].

A massive disruption of the PINP was the prerequisite for induction of sustained AF in our experiments. This incision extensively brought conductive disarray over specific areas of the atrial free wall, presumably with a concomitant decrease in input through these areas, both of which would create a long excitable gap around the RA basis in the presence of the intact AINP. The resultant sustained AF was somewhat modified in frequency by transection of the MINP (the frequency was not always reduced as described by Pastelin and associates [23]), but no longer induced after the AINP was transected. (The section of PINP and MINP did not prevent sustained AF, contrary to the report by Pastelin and associates [23].)

Arrhythmias, primarily persistent JR, have been observed after specific incision patterns, but not after others. As early as 1968, Sealy and associates [2] emphasized the physiological importance of the INP based on experiments using sequential division of the INP to produce JR in 7 of 10 dogs. Hamilton and colleagues [1] described disturbances in atrial conduction and rhythm in 16 of 27 patients subjected to Blalock-Hanlon's procedure. They thought that surgical trauma to the atrial septum with possible injury to the INP might have been the cause of such disturbances. Sealy and associates [2] concluded that at least one INP should be preserved.

Several other experiments have observed the connection between disrupted INP and arrhythmias. Haller and co-workers [5] reported that some type of postoperative dysrhythmia developed in all 9 children undergoing the Mustard procedure. Isaacson and associates [6] described postoperative conduction disturbances in 22 of 23 patients with the Senning operation and in all 14 with the Mustard operation. Junctional rhythm and AV dissociation were the common types of dysrhythmia in both groups. The latter group emphasized the importance of three intact INPs, particularly AINP and MINP, to prevent JR. Wittig and colleagues [7] made intraoperative and perioperative maps of atrial conduction in 38 patients with the Mustard operation and pointed out that excision of the septum and coronary sinus always produced a block in the posterior CT and that placement of a baffle made the block worse.

In our experiments, conduction time from the SA node to the AV node was remarkably delayed after division of the AINP, but there appeared to be little delay even after serious disruption of either the PINP or the MINP. Our observation was similar to those by Holsinger and associates [24]—the AINP is the shortest and probably most important route of excitation [14, 24]. On the other hand, JR developed in about one half of the dogs subjected to disruption of all three pathways, or of the AINP and PINP. Transection of the AINP resulted in a marked conduction delay to the AV node and elongation of the A-H interval, not compensated for by the remaining conduction system. However, disruption of any single pathway alone did not produce persistent JR. It should be of great interest that persistent JR often developed when disruption of the PINP was added to that of the AINP (see Table 2), although disruption of the PINP alone resulted in little delay in the conduction time to the AV node (see Fig 3). Recently we observed prolongation of the A-H interval up to about 10 ms with continuous sinus rhythm in 4 of 5 dogs with CPB subjected to a horseshoe-shaped atriotomy transecting three pathways. Such a prolongation was a prelude to JR in 3 of these 4. These findings strongly suggest that the essential cause in producing JR is the decrease of input to the AV node, which supports the "summation theory" [25–27]. It is also concordant with clinical implications by Wittig and associates [7]. In addition, the results in groups C and D strongly suggest that blockade of atrial feeding arteries causing SA node hypoxia boosts occurrence of JR in the presence of massive injury of preferential routes, particularly the AINP. Corrected sinus node recovery time was often prolonged shortly before onset of JR in those dogs. Anterior INP division should be a potent factor to prolong both A-H internal and corrected sinus node recovery time.

The incidence and type of dysrhythmias after atrial-level intervention in both humans and dogs varied with reporters [1–10, 24]. This may be well explained by our experimental results that such dysrhythmias are caused by the interaction in not only traumatized preferential routes subjected to cicatric changes [10], but also atrial hypoxia jeopardizing the conduction system.

Anatomic and physiologic properties may not be identical between humans and dogs. For example, the distal AINP lies more closely to the distal MINP in humans, as photographically shown by James [14] and Holsinger and associates [24]. Larger or upper atrial secundum defect may further approximate both INPs, as illustrated by Sealy and co-workers [2]. Some divergent opinion may be acceptable for such anatomic reasons due to different species or congenital anomaly. Nevertheless, our canine data well explain the mechanism of postoperative dysrhythmias in our past patients with atrial septal defect. Our conclusion may be useful for the atrial baffling procedure for transposition of the great arteries as well. Our recommendation for preventing postoperative dysrhythmias is to attempt to protect the integrity of at least the AINP and PINP, and also the feeding arteries.

Supported in part by grant-in-aid for scientific research No. B-62480295 from the Japanese Ministry of Education, Science, and Culture.

References

1. Hamilton SD, Bartley TD, Miller RH, Scheibler GL, Marrit HJL. Disturbances in atrial rhythm and conduction following the surgical creation of an atrial septal defect by the Blalock-Hanlon technique. Circulation 1968;38:73–81.
2. Sealy WC, Farmer JC, Young WG Jr, Brown IW Jr. Atrial dysrhythmia and atrial secundum defects. J Thorac Cardiovasc Surg 1969;57:245–50.
3. Haller JA Jr, Crisler C, Brawley R, Cameron J, Rowe RD. Operative correction and postoperative management of transposition of the great vessels in nine children. Ann Thorac Surg 1969;7:212–20.
4. Tamiya T, Suzuki I, Koja K, Liao Y, Ito S, Namikawa M. Reevaluation of persistent arrhythmias following the repair of atrial septal defect. Jpn J Thorac Surg 1972;25:863–71.
5. El-Said G, Rosenberg HS, Mullins CE, Hallman GL, Cooley DA, McNamara DG. Dysrhythmias after Mustard's operation for transposition of the great arteries. Am J Cardiol 1972;30:526–32.
6. Isaacson R, Titus JL, Meredith J, Feldt RH, McGoon DC. Apparent interruption of atrial conduction pathways after surgical repair of transposition of great arteries. Am J Cardiol 1972;30:533–5.
7. Wittig JH, de Leval MR, Stark J, Castaneda A. Intraoperative mapping of atrial activation before, during, and after the Mustard operation. J Thorac Cardiovasc Surg 1977;73:1–13.
8. Lewis AB, Lindesmith GG, Takahashi M, et al. Cardiac rhythm following the Mustard procedure for transposition of the great vessels. J Thorac Cardiovasc Surg 1977;73:919–26.
9. Koike K, Yoshitake K, Naganuma M, Tsunemoto M, Kohno T, Naito T. Lethal arrhythmias in infants and children. Jpn J Pediatr Surg 1980;12:1333–46.
10. Hata J. Pathology of conduction system in the cases of sudden death in late periods following the Mustard procedure. Jpn J Pediatr Surg 1980;12:1383–7.
11. Spach MS, Lieberman M, Scott JG, Barr RC, Johnson EA, Kootsey JM. Excitation sequences of the atrial septum and the AV node in isolated hearts of the dog and rabbit. Circ Res 1971;29:156–72.
12. Frame LH, Page RL, Boyden PA, Fenoglio JJ Jr, Hoffman BF. Circus movement in the canine atrium around the tricuspid ring during experimental atrial flutter and during reentry in vitro. Circulation 1987;76:1155–75.
13. Boyden PA, Frame LH, Hoffman BF. Activation mapping of reentry around an anatomic barrier in the canine atrium: observations during entrainment and termination. Circulation 1989;79:406–16.
14. James TN. The connecting pathways between the sinus node and AV node and between the right and the left atrium in the human heart. Am Heart J 1963;66:498–508.
15. Funada T, Iwase T, Iwa T. Computer extraction of the moment of epicardiac excitation. MBE 1978;78:17–22.
16. Narula OS. His bundle electrocardiography and clinical electrophysiology. 2nd ed. Philadelphia: F.A. Davis, 1977.
17. Lewis T, Feil HS, Stroud WD. Observations upon flutter and fibrillation; part II. The nature of auricular flutter. Heart 1920;7:191–245.
18. Rosenblueth A, Garcia-Ramos J. Studies on flutter and fibrillation: II. The influence of artificial obstacles on experimental auricular flutter. Am Heart J 1947;33:677–84.
19. Lanari A, Lambertini A, Ravin A. Mechanism of experimental atrial flutter. Circ Res 1956;4:282–7.
20. Kimura E, Kato K, Murao S, Ajisaka H, Koyama S, Omiya Z. Experimental studies on the mechanism of the auricular flutter. Tohoku J Exp Med 1954;60:197–207.
21. Frame LH, Page RL, Hoffman BF. Atrial reentry around an anatomic barrier with a partially refractory excitable gap: a canine model of atrial flutter. Circ Res 1986;58:495–511.
22. Boineau JP. Atrial flutter: a synthesis of concepts. Circulation 1985;72:249–57.
23. Pastelin G, Mendez R, Moe GK. Participation of atrial specialized conduction pathways in atrial flutter. Circ Res 1978; 42:386–93.
24. Holsinger JW Jr, Wallace AG, Sealy WC. The identification and surgical significance of the atrial internodal conduction tracts. Ann Surg 1968;167:447–53.
25. Zipes DP, Mendez C, Moe GK. Evidence for summation and voltage dependency in rabbit atrioventricular nodal fibers. Circ Res 1973;32:170–7.
26. Janse MJ, Van Capelle FJL, Anderson RH, Touboul P, Billette J. Electrophysiology and structure of the atrioventricular node of the isolated rabbit heart. In: Wellens HJJ, Lie KI, Janse MJ, ed. The conduction system of the heart. Leiden: Stenfert Kroese BV, 1976:296–315.
27. Sealy WC, Seaber AV. Cardiac rhythm following exclusion of the sinoatrial node and most of the right atrium from the remainder of the heart. J Thorac Cardiovasc Surg 1979;77: 436–47.

Time for New Concepts About Measurement of Complement Activation by Cardiopulmonary Bypass?

Vibeke Videm, MD, PhD, Erik Fosse, MD, PhD, Tom Eirik Mollnes, MD, PhD,
Peter Garred, MD, PhD, and Jan L. Svennevig, MD, PhD

Institute for Experimental Medical Research and Department of Surgery, Ullevaal Hospital, and Institute of Immunology and Rheumatology, The National Hospital, Oslo, Norway

Fifty-one patients admitted for routine coronary bypass operations were randomized to cardiopulmonary bypass with a membrane oxygenator (Capiox) or a bubbler (Polystan or William Harvey). Complement activation was measured using enzyme immunoassays for concentrations of C3 activation products and the terminal complement complex. From 5.8 to 8.1 arbitrary units (AU)/mL (medians), the plasma concentrations of C3 activation products increased by 119.9 AU/mL (Capiox), 124.6 AU/mL (Polystan), and 79.5 AU/mL (William Harvey) to a peak at closure of the sternum (not significant when related to baseline concentrations). The increase in C3 activation products and baseline C3 activation were linearly correlated ($R^2 = 0.30$; $p < 0.0001$). From 5.5 to 6.1 AU/mL, the plasma terminal complement complex concentrations increased by 45.2 AU/mL (Capiox), 15.4 AU/mL (Polystan), and 17.4 AU/mL (William Harvey) to a peak before termination of cardiopulmonary bypass. Maximal terminal (C5–C9) activation was significantly higher in the membrane oxygenator group ($p < 0.0001$) and showed no relationship to C3 activation. Measurement of C3 activation only gives no information about C5–C9 activation. At present, terminal complement complex quantitation is probably the best index of C5–C9 activation during cardiopulmonary bypass.

(Ann Thorac Surg 1992;54:725–31)

The term *biocompatibility* is often used to describe the body's inflammatory reaction to different forms of extracorporeal circulation, such as cardiopulmonary bypass (CPB), hemodialysis, and apheresis techniques. There is strong evidence that activated complement factors that are formed during contact between blood and foreign surfaces may have adverse effects when released into the circulation, both directly by affecting the heart, pulmonary circulation, and inducing hemolysis and indirectly by activating granulocytes and monocytes with subsequent release of other inflammatory mediators. Therefore, the degree of complement activation induced by extracorporeal circulation has been proposed as an index of its biocompatibility [1]. The clinical relevance of this index is supported by studies showing significant correlation with organ dysfunction after CPB [2] and adverse symptoms during hemodialysis [3].

Membrane oxygenators are often regarded as more biocompatible than bubblers, partly due to less blood traumatization. We have previously found that complement activation in vitro depended on non–material-related properties of the specific CPB oxygenator [4]. Presumably both the size of the foreign surface area and the manner of blood flow within the oxygenator were of importance. We also demonstrated that a spiral coil silicone membrane oxygenator was a more potent C3 activator than bubblers in vivo [5]. The degree of both platelet activation and granulocyte degranulation is larger with spiral coil than with hollow fiber membrane oxygenators [6, 7], which may indicate that flow conditions in the previously tested membrane oxygenator were especially unfavorable. In the present follow-up study, in vivo complement activation was therefore compared using three different oxygenators, one of which was a hollow fiber membrane oxygenator. To further investigate the role of direct oxygen bubbling into the blood, a new hybrid of a bubble and a film oxygenator was included, in which gas is bubbled through oxygenating tubes that also transport the blood. A collapsible bubbler known to be a moderate complement activator was retested, serving as a control and means for comparison with the previous investigation.

Material and Methods

Patients and Procedures

Fifty-one patients (43 men and 8 women) admitted for routine coronary bypass operations were included after giving informed consent. Inclusion criteria were left ventricular ejection fraction of 0.40 or greater, absence of major noncardiac illness, normal liver function, and no history of recent steroid use. Aspirin treatment was dis-

---

Accepted for publication Feb 19, 1992.

Address reprint requests to Dr Videm, Institute for Experimental Medical Research, Ullevaal Hospital, N-0407 Oslo 4, Norway.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Patient Characteristics and Variables Pertaining to Operation[a]

Parameter	Group		
	Capiox	Polystan	William Harvey
Age (y)	59 (53–63)	59 (65–63)	61 (58–63)
Sex (male/female)	11/2	21/3	11/3
Preop LVEF	0.60 (0.53–0.64)	0.60 (0.55–0.64)	0.62 (0.58–0.66)
No. of grafts	2.5 (2–3)	2.5 (2–3)	2.5 (2–3)
Operation time (min)	182 (161–208)	206 (187–225)	204 (177–235)
CPB time (min)	86 (66–96)	95 (82–108)	89 (79–100)
Aortic occlusion time (min)	42 (32–50)	53 (42–58)	46 (31–53)

[a] Values are medians and 95% nonparametric confidence intervals. The differences among the groups were not statistically significant for any parameter (Kruskal-Wallis test).

CPB = cardiopulmonary bypass; LVEF = left ventricular ejection fraction.

continued 8 days preoperatively. By the closed envelope method, patients were randomly assigned to CPB with one of the following oxygenators: The polypropylene hollow fiber membrane Capiox E (Terumo Corporation, Tokyo, Japan) (n = 13), the collapsible bubbler Polystan VT-11500 (Polystan, Copenhagen, Denmark) (n = 24), and the hybrid bubbler William Harvey H-1700 (C. R. Bard, Santa Ana, CA) (n = 14). An arterial line depth blood filter (Cobe Laboratories, Lakewood, CO) and a nonpulsatile roller pump (Gambro, Horten, Norway) were used for all operations.

The extracorporeal circuit was primed with 2,500 mL of a standard mixture of dextran 70 (60 mg/mL in saline solution), Ringer's acetate, glucose (50 mg/mL), mannitol (150 mg/mL), and sodium hydrogen carbonate (500 mmol/L). Anesthesia was maintained with thiopental, diazepam, fentanyl, pancuronium, and nitrous oxide. Heparin was given intravenously at a dose of 4 mg/kg body weight before onset of CPB. If necessary, additional heparin was administered to maintain an activated clotting time greater than 480 seconds. Cold St. Thomas' cardioplegia was used in addition to local cooling and moderate general hypothermia (30° to 32°C). No steroids were administered. Cardiotomy suction was used during all operations. Protamine dosage was twice the heparin dose, and additional protamine was given if needed to reestablish prebypass activated clotting time levels.

Duration of the operation, CPB, and aortic occlusion was recorded. Blood samples anticoagulated with EDTA were obtained at induction of anesthesia (ie, baseline), at the start of the operation, immediately before CPB, after 30 and 60 minutes of CPB, during closure of the sternum, every 4 hours postoperatively for 24 hours, and every 6 hours for the next 24 hours. All samples were kept on ice for a short period until analysis or centrifugation. Plasma was stored at −70°C. There were no differences among the three patient groups with respect to preoperative medication, number of previous cardiac infarctions, location of or number of coronary artery stenoses, or concomitant vascular disease such as hypertension or intermittent claudication. The three groups were also comparable with respect to the patient characteristics and variables pertaining to the operation, as shown in Table 1.

The study conformed with the ethical guidelines of the Helsinki declaration and was approved by the regional ethical committee.

Analyses of Samples

C3 activation was measured in a double antibody enzyme immunoassay (EIA) specific for a C3 neoepitope (ie, antigenic determinant present in activation products, but not in the native component) expressed on C3b, iC3b, and C3c [8]. The terminal SC5b-9 complement complex (TCC) was quantified in a similar EIA [9] specific for a neoepitope expressed only in activated C9. In both assays zymosan-activated serum was used as a standard, defined as containing 1,000 arbitrary units (AU)/mL, because the use of SI units requires that the neoepitope be confined to one particular protein. All complement measurements were done in triplicate and gave closely correlated results.

The hemoglobin concentrations in the samples were determined in an electronic counter (Coulter Electronics, Harkenden, England). The results were corrected for hemodilution during CPB by multiplication with the factor: initial hemoglobin/sample hemoglobin. The degree of hemodilution was equivalent in all three oxygenator groups ($p > 0.2$). Statistical comparison among the groups gave similar results whether performed on uncorrected or corrected data.

Statistics

Nonparametric statistical methods were used due to nonnormal distribution of variables. Values of p less than 0.05 were considered statistically significant. Results are presented as median based on Walsh numbers with 95% nonparametric confidence intervals in parentheses. The Friedman test [10] was used for statistical analyses of time-dependent parameter changes within each group. The Kruskal-Wallis test [10] was applied for intergroup comparisons of peak complement activation, and repeated measurements analysis of variance was performed on ranks [10] to assess whether the complement activation curves from the three groups were significantly different from immediately before onset of CPB to closure of the sternum. Linear regression was done with standard methods in the SPSS-PC$^+$ computer program package.

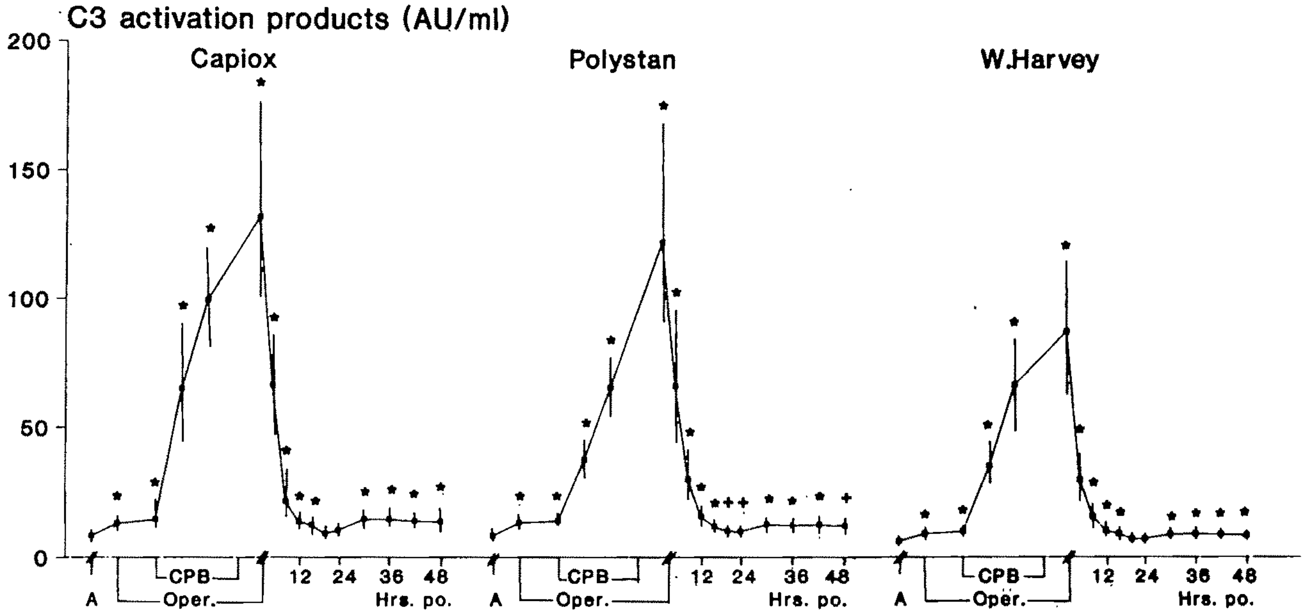


Fig 1. Concentration of C3 activation products during coronary bypass operations with three different oxygenators and during the first 48 postoperative hours (median and 95% confidence intervals). Note change in scale on x-axis. Significant change from baseline sample at induction of anesthesia: $^+p < 0.05$, $^*p < 0.001$ *(Friedman test). (A = induction of anesthesia; CPB = time on cardiopulmonary bypass,* Hrs.po. = *hours postoperatively;* Oper. = *operation.)*

Results

The baseline concentrations of C3 activation products were significantly lower in the William Harvey group ($p < 0.05$). The concentrations of C3 activation products increased in an almost linear fashion from the onset of CPB in all three oxygenator groups (Fig 1). After reaching a peak at closure of the sternum, the C3 activation products returned to levels comparable with baseline approximately 20 hours postoperatively.

When related to baseline concentrations, C3 activation after 60 minutes on CPB was somewhat lower in the Polystan group than the Capiox group (Capiox, 12.4 [10.1–15.0]; Polystan, 8.4 [6.9–10.1]; William Harvey, 11.0 [9.0–12.9] times baseline C3 activation, respectively; Polystan versus Capiox, $p < 0.05$; other comparisons not significant). The increase in C3 activation products from baseline to the peak was 119.9 (98.5–153.8) AU/mL in the Capiox group, 125.6 (93.7–165.9) AU/mL in the Polystan group, and 79.5 (60.4–103.0) AU/mL in the William Harvey group (William Harvey versus Capiox or Polystan, $p < 0.05$) (Fig 2A, Table 2). When related to the baseline concentrations, the apparent lower C3 activation with the latter oxygenator was no longer present ($p = 0.64$) (Fig 2B). In the total group of 51 patients, a significant linear correlation was found between the increase in C3 activation products from baseline to the peak and baseline C3 activation ($R^2 = 0.30$; $p < 0.0001$) (Fig 3).

The concentrations of TCC also increased almost linearly from the onset of CPB (Fig 4). A peak was reached before termination of CPB, ie, before administration of protamine, and the TCC concentrations returned to levels not significantly different from baseline between 8 and 12 hours postoperatively. The increase in TCC from baseline to the peak was 45.2 (32.3–58.3) AU/mL in the Capiox group, 15.4 (12.4–22.3) AU/mL in the Polystan group, and 17.4 (15.0–25.6) AU/mL in the William Harvey group (Capiox versus Polystan or William Harvey, $p < 0.0001$) (Fig 5A). Repeated-measurements analysis of variance confirmed that TCC formation was significantly higher in the Capiox group from immediately before onset of CPB to closure of the sternum ($p = 0.001$). The differences in maximal increases of TCC were not related to baseline concentrations of TCC (Fig 5B). There was no systematic relationship between maximal increases from baseline in C3 activation products and TCC in the 51 patients (Fig 6).

Comment

In the present study of complement activation during and after coronary bypass operations, peak increases in C3 activation products were correlated with baseline concentrations and unrelated to the type of oxygenator used. Terminal complement activation, measured as changes in TCC, was significantly higher with a hollow fiber membrane oxygenator than with a collapsible or a hybrid bubbler.

In a previous study of CPB employing the same complement activation analyses, we found significantly higher C3 activation with a spiral coil membrane oxygenator than with a collapsible bubbler (the same Polystan brand as used in the present study) or a hard shell bubbler [5]. Taken together, these two studies clearly demonstrate that a membrane oxygenator, whether spiral coil or hollow fiber, is not necessarily advantageous to the patients with respect to biocompatibility during relatively short-lasting perfusions. From a clinical point of view, terminal (C5–C9) complement activation is probably the more

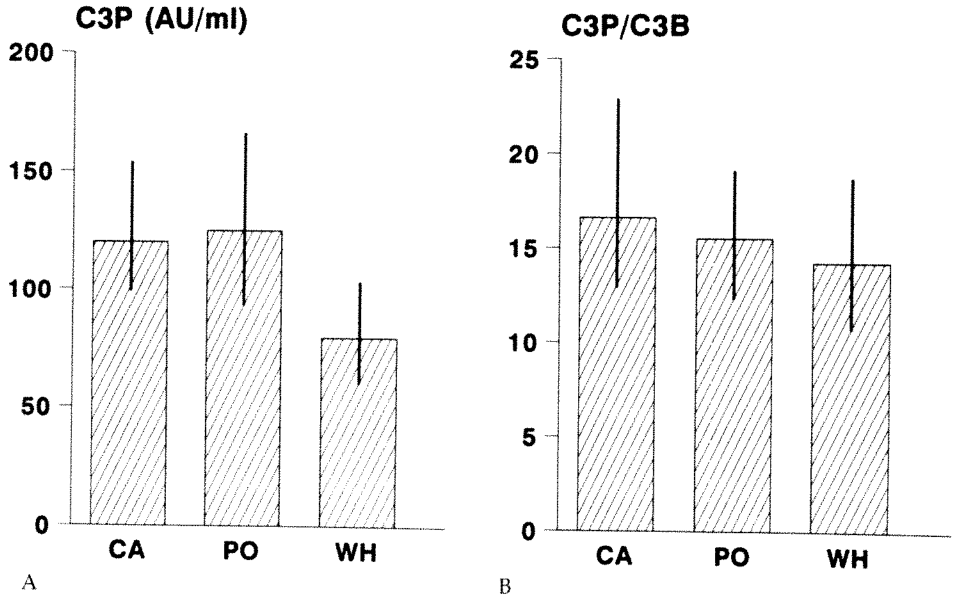


Fig 2. Changes in concentrations of C3 activation products during coronary bypass operations with three different oxygenators (median and 95% confidence intervals). (A) Peak increase from baseline (C3P). *WH versus CA or PO,* $p < 0.05$. *CA versus PO, not significant (Kruskal-Wallis test). (B) Peak increase from baseline divided by baseline value* (C3P/C3B). *No significant differences among groups.* (CA = *Capiox;* PO = *Polystan;* WH = *William Harvey.)*

important parameter, because the pathogenesis of the "whole-body inflammatory reaction" after CPB is likely to involve activation of granulocytes and monocytes by the complement activation product C5a [2].

In a previous study comparing complement activation between bubble and membrane oxygenators during short-term perfusions, no difference was found in consumption of native C3 or C4 [11]. However, measurement of changes in native complement factors is a much less sensitive method than quantitation of increases in activation fragments [1]. Less than 10% of total native C3 is converted during CPB. Baseline (spontaneous) C3 activation, on the other hand, is very small, so that the increase in C3 activation products is often tenfold or more.

The present study further confirms that even though vigorous bubbling of pure oxygen through blood activates complement in vitro [12], the blood-gas interface in bubble oxygenators of different construction does not play an important role for overall complement activation in vivo. According to the manufacturer of the hybrid bubbler, a smaller gas volume and bubble size due to so-called wall-stabilized flow within the oxygenating tubes in this oxygenator diminishes turbulence and blood trauma. This did not result in reduced complement activation as compared with the collapsible bubbler.

It is well known that complement activation is higher in plasma from certain donors when exposed to a standardized activating stimulus in vitro [3], reflecting a higher "immunological reactivity." In this study, we report a correlation between the spontaneous level of C3 activation as reflected in the baseline samples and the peak increase during CPB. The baseline concentrations of C3 activation products accounted for almost one third of the variation in peak activation during CPB. However, this correlation needs to be confirmed in other studies.

Bhakdi and co-workers [13] demonstrated that during complement activation induced by Sephadex beads, which is a foreign surface resulting in alternative pathway

Table 2. Effect of Hemodilution on Peak Complement Activation[a]

Parameter	Group		
	Capiox	Polystan	William Harvey
C3 activation products (AU/mL)			
Uncorrected	79.5 (65.0–105.5)	76.0 (57.6–105.3)	52.3 (40.9–65.2)
Corrected	119.9 (98.5–153.8)	125.6 (93.7–165.9)	79.5 (60.4–103.0)
Terminal complement complex (AU/mL)			
Uncorrected	24.2 (17.0–32.2)	8.1 (6.2–11.8)	9.8 (7.0–12.3)
Corrected	45.2 (32.3–58.3)	15.4 (12.4–22.3)	17.4 (15.0–25.6)

[a] Values are peak increases from baseline at induction of anesthesia (median and 95% nonparametric confidence interval). Uncorrected data are plasma concentrations, corrected data are plasma concentrations multiplied with the factor, initial hemoglobin concentration/sample hemoglobin. The degree of hemodilution was equivalent in all groups ($p > 0.2$).

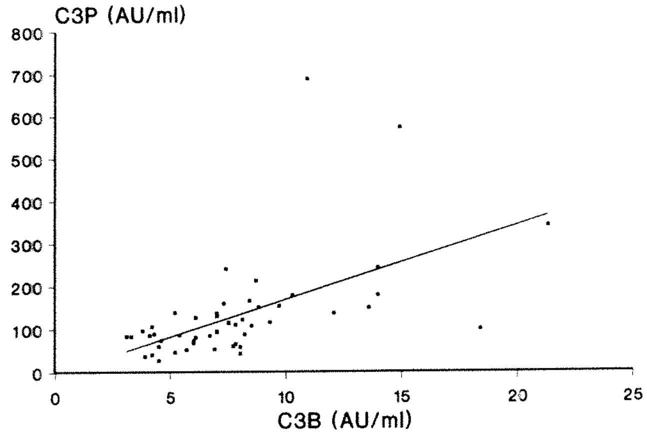


Fig 3. Peak increase in C3 activation products from baseline (C3P) plotted versus baseline concentrations (C3B) for 51 patients undergoing coronary bypass operations. Linear regression line is indicated ($R^2 = 0.30$; $p < 0.0001$).

activation, the molar ratio of C3a:C5a generation was approximately 30:1 and of C5a:TCC generation near 1.2:1. With antibody-antigen complexes inducing classic complement activation, as do heparin-protamine complexes during CPB [14], C3a:C5a generation ranged from 60 to 200:1 and C5a:TCC generation from 1 to 30:1. These findings may explain why the TCC peak occurred before the C3 activation peak in our patients, as C3 activation is likely to further have increased after administration of protamine with only little concomitant formation of TCC.

From the stated findings of Bhakdi and co-workers [13] it is clear that regulation of the complement cascade varies with the nature of the activating stimulus, and that formation of a certain amount of C3a may result in generation of widely varying amounts of C5a or TCC. These facts are reflected in the present study, where no relationship between peak C3 activation and terminal activation could be detected. Our findings cause concern about the present way in which complement activation is most often measured in evaluation of biocompatibility of CPB.

Gardinali and co-workers [1] have recommended the use of C3a radioimmunoassay (RIA) alone as a test of biocompatibility during CPB. Even if a correlation of C3a concentrations and postoperative organ dysfunction has been shown after CPB [2], it seems that this recommendation to a great extent is a consequence of the methodological problems that arise when only the commercially available C5a RIA is considered for quantitation of terminal complement activation. Measurements of C5a during CPB with this RIA have seldom given useful information about CPB because C5a is bound to receptors on granulocytes and monocytes within minutes after formation [1], and the lower detection limit of the C5a RIA is 10 ng/mL. Using a novel EIA that is highly specific and detects C5a concentrations as low as 10 pg/mL, we recently showed that considerable amounts of C5a/C5a desArg were actually generated in plasma during CPB [15]. Due to the kinetics of C5a/C5a desArg with possible release of cell-bound C5a and degradation products postoperatively, the novel assay seems most useful in vitro. However, our study indicates that important information about the terminal part of the complement cascade is likely to be overlooked when only C3 activation is quantitated. At present, measurement of TCC is probably the best marker of C5–C9 activation during CPB, even if the concentra-

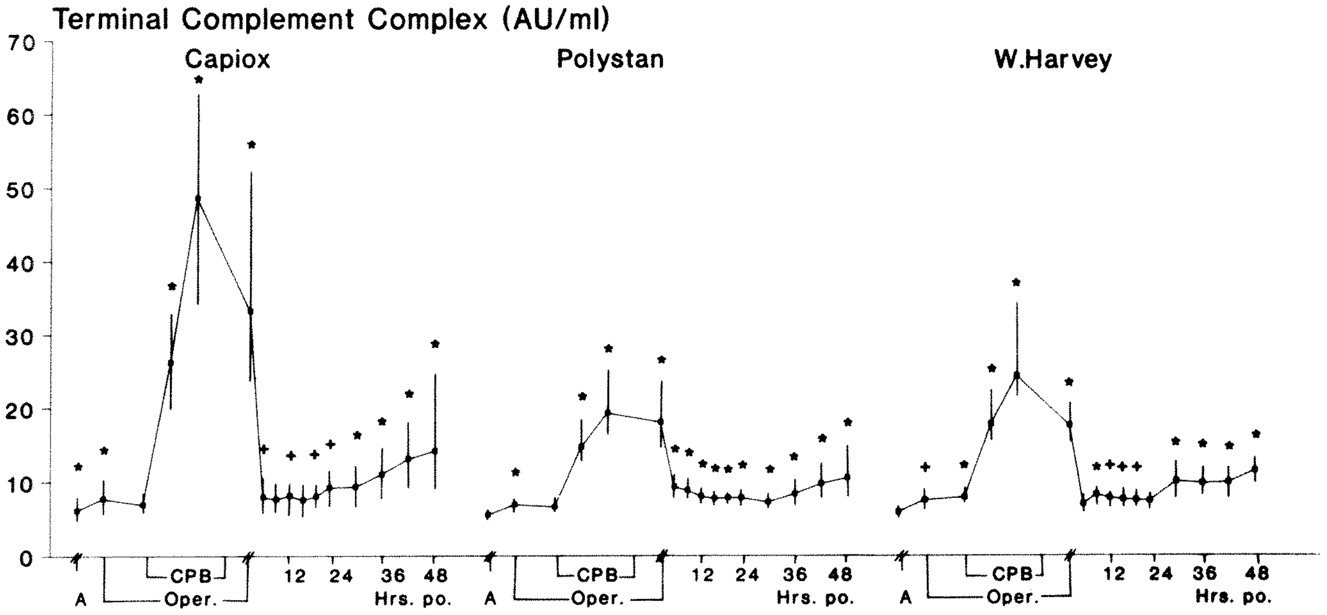


Fig 4. Concentration of terminal C5–C9 complement complex during coronary bypass operations with three different oxygenators and during the first 48 postoperative hours (median and 95% confidence intervals). Note change in scale on x-axis. Significant change from baseline sample at induction of anesthesia: $^{+}p < 0.05$; $^{*}p < 0.001$ *(Friedman test). (Abbreviations as in Figure 1.)*

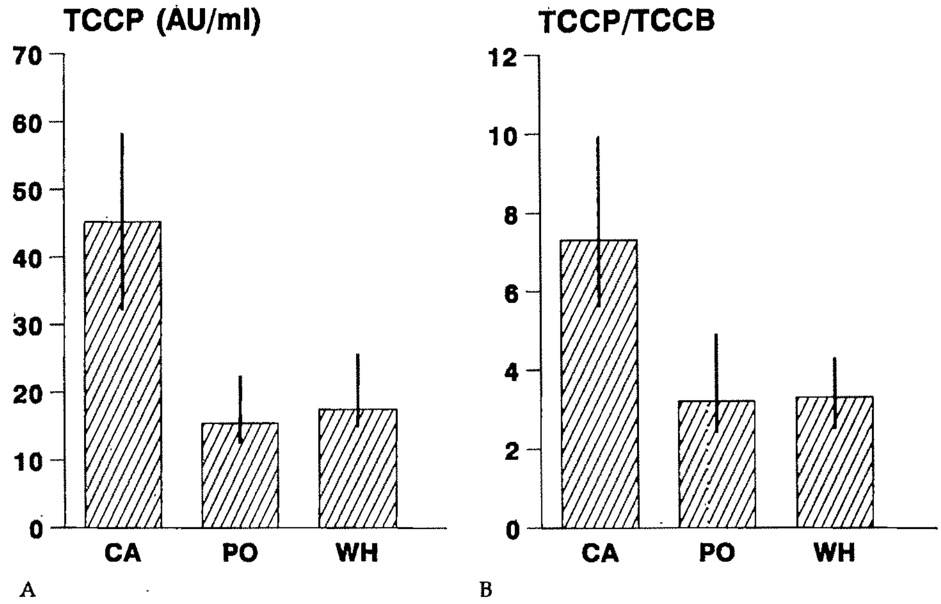


Fig 5. Changes in terminal C5–C9 complement complex concentrations during coronary bypass operations with three different oxygenators (median and 95% confidence intervals). (A) Peak increase from baseline (TCCP). CA versus PO or WH, $p < 0.0001$. PO versus WH, not significant (Kruskal-Wallis test). (B) Peak increase from baseline divided by baseline value (TCCP/TCCB). CA versus PO or WH, $p < 0.001$. PO versus WH, not significant. (CA = Capiox; PO = Polystan; WH = William Harvey.)

tions of C5a formed may have been higher than reflected in the TCC concentrations. Terminal complement complex is easily measured in EIA [16], and has a half-life in plasma of approximately ½ to 1 hour [16, 17]. In a study of hemodialysis with different membranes, Deppisch and co-workers [17] recently found that TCC was a sensitive marker of biocompatibility. Terminal complement complex quantitation (EIA) gave a higher ratio of maximal versus basal concentrations than did C3a and C5a measurements (RIA), and for one of the membranes complement activation was detected only when using the TCC assay.

However, the body's reaction to contact between blood and foreign surfaces includes not only complement activation, but also activation of leukocytes, platelets, and the coagulation, fibrinolytic, and plasma kallikrein-kinin systems. Using complement activation alone as an index of CPB biocompatibility thus gives fragmentary information. Yet, complement activation during cardiac operations before onset of CPB is at most minor and is not significantly increased by the thoracotomy itself [18], whereas the substantial activation of the plasma kallikrein-kinin and fibrinolytic systems caused by intravenous administration of heparin [19, 20] render evaluation of the CPB-related component difficult.

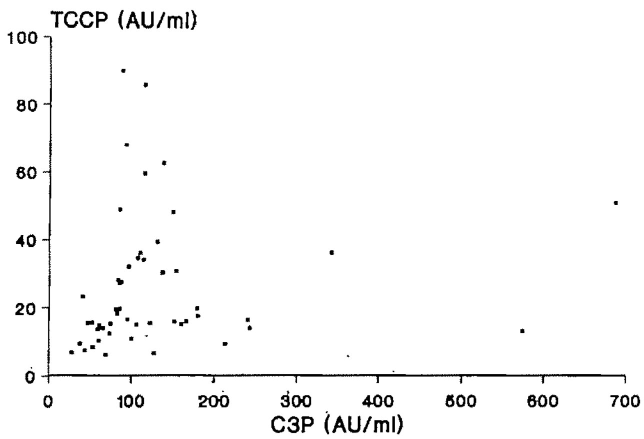


Fig 6. Peak increase in concentration of terminal C5–C9 complement complex from baseline (TCCP) plotted versus peak increase in C3 activation products (C3P) for 51 patients undergoing coronary bypass operations.

During hemodialysis, a standard method to classify biocompatibility has been a combined approach, namely to assay the concentrations of C3a in an RIA and calculate the decreases in numbers of circulating granulocytes [21]. The more incompatible dialysis membranes activate C3 and lead to a profound granulocyte drop, the membranes in an intermediate group are moderate C3 activators but still induce granulocytopenia, and the more biocompatible membranes barely activate C3 and induce only small changes in granulocyte counts. However, a classification including changes in granulocyte counts is not useful during CPB. First, the degree of degranulation and release of inflammatory mediators was significantly different in two model CPB set-ups where the granulocyte drop was equivalent [22]. Second, we found significant differences in C3 activation products measured in EIA during in vivo CPB, whereas the granulocyte counts were similar [5]. Thus, as opposed to the situation during hemodialysis, only a parameter showing the degree of degranulation seems justified when including granulocytes in biocompatibility studies of CPB.

We conclude that complement activation is useful when investigating the biocompatibility of CPB, provided that activation products at both the C3 level and the C5–C9 level are quantitated. A combined approach also including measurements of leukocyte and platelet activation may prove better than assessment of the complement cascade alone, but a standard "biocompatibility index" has not yet been defined. Ultimately, the usefulness of any biocompatibility index depends on its correlation with clinical outcome in studies with a large number of patients.

Hans Nielsen, Grethe Bergseth, Bente Falang, and the staff of the Surgical Department Laboratory of Ullevaal Hospital are acknowledged for excellent technical assistance.

This study was supported by Anders Jahre's Fund for the Promotion of Science, The Norwegian Council on Cardiovascular Research, the Nordic Insulin Foundation, and the Norwegian Research Council for Science and the Humanities.

References

1. Gardinali M, Circardi M, Agostoni A, Hugli TE. Complement activation in extracorporeal circulation: physiological and pathological implications. Pathol Immunopathol Res 1986;5:352–70.
2. Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–57.
3. Hakim RM, Breillatt J, Lazarus JM, Port FK. Complement activation and hypersensitivity reactions to dialysis membranes. N Engl J Med 1984;311:878–82.
4. Videm V, Fosse E, Mollnes TE, Ellingsen Ø, Pedersen T, Karlsen H. Different oxygenators for cardiopulmonary bypass lead to varying degrees of human complement activation in vitro. J Thorac Cardiovasc Surg 1989;97:764–70.
5. Videm V, Fosse E, Mollnes TE, Garred P, Svennevig JL. Complement activation with bubble and membrane oxygenators in aortocoronary bypass grafting. Ann Thorac Surg 1990;50:387–91.
6. Addonizio VP. Platelet function in cardiopulmonary bypass and artificial organs. Hematol Oncol Clin North Am 1990;4:145–55.
7. Stahl RF, Fisher CA, Kucich U, et al. Effects of simulated extracorporeal circulation on human leukocyte elastase release, superoxide generation, and procoagulant activity. J Thorac Cardiovasc Surg 1991;101:230–9.
8. Garred P, Mollnes TE, Lea T. Quantification in enzyme-linked immunosorbent assay of a C3 neoepitope expressed on activated human complement factor C3. Scand J Immunol 1988;27:329–35.
9. Mollnes TE, Lea T, Frøland SS, Harboe M. Quantification of the terminal complement complex in human plasma by an enzyme-linked immunosorbent assay based on monoclonal antibodies against a neoantigen of the complex. Scand J Immunol 1985;22:197–202.
10. Conover WJ. Practical non-parametric statistics. 2nd ed. New York: Wiley, 1980:229–37, 299–308, 337.
11. Mickleborough LL, Arnold G, Chiu RC-J. Complement consumption during cardiopulmonary bypass: bubble versus membrane oxygenators. Perfusion 1986;1:261–9.
12. Tamiya T, Yamasaki M, Maeo Y, Yamashiro T, Ogoshi S, Fujimoto S. Complement activation in cardiopulmonary bypass, with special reference to anaphylatoxin production in membrane and bubble oxygenators. Ann Thorac Surg 1988;46:47–57.
13. Bhakdi S, Fassbender W, Hugo F, et al. Relative inefficiency of terminal complement activation. J Immunol 1988;141:3117–22.
14. Cavarocchi NC, Schaff HV, Orszulak TA, Homburger HA, Schnell WA, Pluth JR. Evidence for complement activation by protamine-heparin interaction after cardiopulmonary bypass. Surgery 1985;98:525–31.
15. Mollnes TE, Videm V, Götze O, Harboe M, Oppermann M. Formation of C5a during cardiopulmonary bypass: inhibition by precoating with heparin. Ann Thorac Surg 1991;52:92–7.
16. Mollnes TE. Early- and late-phase activation of complement evaluated by plasma levels of C3dg and the terminal complement complex. Complement 1985;2:156–64.
17. Deppisch R, Schmitt V, Bommer J, Hänsch GM, Ritz E, Rauterberg EW. Fluid phase generation of terminal complement complex as novel index of bioincompatibility. Kidney Int 1990;37:696–706.
18. Fosse E, Mollnes TE, Ingvaldsen B. Complement activation during major operations with or without cardiopulmonary bypass. J Thorac Cardiovasc Surg 1987;93:860–6.
19. Kongsgaard UE, Smith-Erichsen N, Geiran O, Amundsen E, Mollnes TE, Garred P. Different activation patterns in the plasma kallikrein-kinin and complement systems during coronary bypass surgery. Acta Anaesthesiol Scand 1990;33:343–7.
20. Kongsgaard UE, Smith-Erichsen N, Geiran O, Bjørnskau L. Changes in the coagulation and fibrinolytic systems during and after cardiopulmonary bypass surgery. Thorac Cardiovasc Surg 1989;37:158–62.
21. Chenoweth DE. Complement activation in extracorporeal circuits. Ann NY Acad Sci 1987;516:306–13.
22. Videm V, Nilsson L, Venge P, Svennevig JL. Reduced granulocyte activation with a heparin coated device in an in vitro model of cardiopulmonary bypass. Artif Organs 1991;15:90–5.

Congenital Malformations of the Coronary Arteries: The Texas Heart Institute Experience

Eugene D. Fernandes, MD, Hooshang Kadivar, MD, Grady L. Hallman, MD,
George J. Reul, MD, David A. Ott, MD, and Denton A. Cooley, MD

Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas

Coronary artery anomalies, some of which are considered clinically insignificant, can be associated with other congenital heart defects, myocardial ischemia, and reduced life expectancy. We conducted a retrospective study to determine the efficacy of surgical treatment in 191 patients who had a total of 202 coronary artery anomalies, which were classified as anomalies of origin (88 patients), termination (93), or distribution (10). Of the 88 patients with anomalies of origin, 60 had a coronary artery arising from the pulmonary artery, 18 had a right coronary artery arising from the left anterior descending artery, and 10 had a coronary artery arising from the contralateral sinus of Valsalva. All patients with an anomaly of termination had a coronary arteriovenous fistula, and all patients with an anomaly of origin had a single coronary artery. The diagnostic and operative techniques for each of the defects are evaluated. Based on our experience, early diagnosis and surgical intervention can yield satisfactory results in patients with coronary artery anomalies, with most experiencing relief of symptoms. The operative procedures were associated with a low early and late mortality; in addition, few patients experienced complications.

(Ann Thorac Surg 1992;54:732–40)

Congenital anomalies of the coronary arteries occur in 1% to 2% of the population [1]. In addition to making angiographic visualization of the coronary circulation more difficult, these congenital anomalies may increase the risk of coronary artery trauma during surgical procedures. Moreover, certain types of anomalies may also produce myocardial ischemia [2]. Nonetheless, state-of-the-art echocardiography and angiography make early detection and accurate delineation of these rare coronary anomalies easier, and modern surgical techniques, including the routine use of cardioplegia, allow most of these anomalies to be corrected.

Patients and Methods

This retrospective study reviews major and certain clinically significant minor anomalies of the coronary arteries diagnosed and treated by the Texas Heart Institute physicians at Texas Children's Hospital and St. Luke's Episcopal Hospital from 1964 to 1989. One hundred ninety-one patients with 202 anomalies were studied. Anomalies were classified into three groups: anomalies of origin, anomalies of termination, and anomalies of distribution (Table 1).

Anomalies of Origin

Eighty-eight patients had anomalies of origin, which included origin of a coronary artery from the pulmonary artery (PA), origin of the left anterior descending artery (LAD) from the right coronary artery (RCA), and origin of a coronary artery from the contralateral sinus of Valsalva.

Patients' ages ranged from 1 month to 53 years, and the group was almost evenly split between the sexes.

Of the 60 cases in which a coronary artery originated from the PA or one of its major branches, 56 (93.3%) involved the left coronary artery (LCA) (Table 2).

Two patients (3.57%) were totally asymptomatic and had only a continuous murmur and electrocardiographic (ECG) changes. In the remaining patients, the predominant symptoms were dyspnea (78.57%) and angina (62.50%). Sixteen patients (28.57%) had congestive cardiac failure. Fourteen of these patients (87.50%) were less than 10 years old, and 7 (43.75%) were less than 1 year old. In neonates and infants, angina was observed to occur at the time of feeding, the so-called "angina of feeding" induced by the effort of sucking [3]. Ten patients (17.85%) had arrhythmias.

Thirteen patients were found to have associated cardiac lesions: mitral regurgitation (7 patients), ventricular septal defect (2), tetralogy of Fallot (2), aortic stenosis (1), and occlusion of the iliac veins resulting from cardiac catheterization (1). On physical examination, 23 patients (41.07%) had a continuous murmur along the left sternal border, heard best in the second and third intercostal spaces. In 15 patients (26.79%), only a systolic murmur was heard. Ischemic changes (ST depression and T-wave inversion) were observed in the anterior and lateral leads in 36 patients (64.28%). Twenty patients showed an infarction pattern with Q waves, with or without ST-T

Accepted for publication Feb 20, 1992.

Address reprint requests to Dr Hallman, PO Box 20345, Houston, TX 77225-0345.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Congenital Anomalies of the Coronary Arteries

Anomaly Type	Patients (n = 191)
Origin	
Origin of a coronary artery from the pulmonary artery	60
Origin of the left anterior descending artery from the right coronary artery	18
Origin of a coronary artery from the contralateral sinus of Valsalva	10
Termination	
Coronary arteriovenous fistula	93
Distribution	
Single coronary artery	10

changes, and 10 of these had cardiac failure. Chest roentgenographic examination revealed in 24 patients (42.85%) evidence of cardiomegaly (cardiothoracic ratio range, 0.51 to 0.73). Echocardiography indicated dilated left ventricles with poor contractility and wall-motion abnormalities in 19 patients (33.92%).

Five patients (8.92%) had dilated left atria and left ventricular hypertrophy. In 3 patients (5.30%), echocardiography detected a dilated and tortuous RCA with collaterals to the LCA. Preoperative cardiac catheterization and coronary angiography were done in all cases and documented elevated preangiographic left ventricular end-diastolic pressure in 18 patients (32.14%), with values ranging from 8 to 26 mm Hg. In 36 patients (64.2%), there was an increase in the oxygen saturation of the PA, indicating a left-to-right shunt. In these 36 patients, angiography revealed a large, dilated RCA with tortuous dilated collaterals and retrograde filling of the LAD. In 4 patients, the collaterals were profuse and large, appearing angiomatous. Mitral incompetence was seen in 7 patients (12.5%); in 3 patients it was severe. In 2 patients, the proximal LCA was dilated with a membranous obstruction at the origin of the circumflex coronary artery. Of the 4 remaining cases in which a coronary artery originated in a PA, 2 were cases in which the RCA arose from the PA, and 2 were cases in which a branch of the LCA arose from the right PA. In the first 2 cases, both patients were men in their twenties, and both had exertional chest pain and dyspnea, with no evidence of congestive cardiac failure. A continuous murmur, indicating good collateral flow from the LCA into the RCA, was heard in both, and electrocardiograms showed evidence of myocardial ischemia in the right-sided and inferior leads. Selective coronary angiography revealed an RCA originating from the main PA with large collaterals filling retrogradely from the LCA.

Table 2. Origin of a Coronary Artery From the Pulmonary Artery: Patient and Sex Distribution

Anomaly	No. (n = 60)	Male (n = 26)	Female (n = 34)
Left coronary artery arising from pulmonary artery	56	23	33
Right coronary artery arising from pulmonary artery	2	2	0
Left atrial branch arising from right pulmonary artery	1	1	0
Circumflex coronary artery arising from right pulmonary artery	1	0	1

Of the 2 patients in whom a branch of the LCA arose from the right PA, 1 had tetralogy of Fallot and had an atrial branch of the LCA arising from the right PA. In the other patient, who also had aortic stenosis, the circumflex branch of the LCA arose from the right PA at its departure from the main PA. The second largest subset of patients with congenital anomalies in the origin of coronary arteries was made up of 18 patients in whom the LAD originated from the RCA. These patients, all children ranging in age from 1 month to 10 years, also had an associated and usually complex congenital heart defect. Of these 12 boys and 6 girls, 15 (83.33%) had tetralogy of Fallot. The remaining 3 had ventricular septal defect and pulmonary stenosis, 1 with atrial septal defect and the other 2 with double-outlet right ventricle.

Finally, there were 10 patients, ranging in age from 2 to 45 years, whose coronary artery arose from the contralateral sinus of Valsalva. In 6, the RCA arose from the left coronary sinus from a separate ostium. Four of these patients were male and 2 were female. In 5, the RCA ran posterior to the aorta to reach the atrioventricular groove, and in 1 it ran between the aorta and the PA. All patients' chief complaint was exertional chest pain, and all had ECG evidence of myocardial ischemia.

In the other 4 patients (3 men and 1 woman), the circumflex coronary branch of the LCA arose from the right coronary sinus from a separate ostium. From this anomalous origin, the vessel ran between the aorta and pulmonary artery to reach the atrioventricular groove and the posterior aspect of the left ventricle, where it was distributed normally. Two of these patients had, in addition, ostial stenosis. One patient had third-degree mitral regurgitation. All complained of angina, especially precipitated by sudden exertion, and all had evidence of ECG changes.

Anomalies of Termination

Ninety-three patients were treated for 104 coronary arteriovenous fistulas (CAVFs) during the 25-year period. The youngest of the 41 male and 52 female patients was 4 days old, and the oldest was 78 years old.

A single fistula was present in 83 patients (89.25%), and multiple fistulas were present in 10 (10.75%). The RCA was the most common vessel of origin, and the most frequent drainage site was the right ventricle (Table 3). The rarest drainage sites were the coronary sinus and the bronchial vein. Three patients suffered aneurysmal dilatations, and in 3 other cases, the fistula became angiomatous. In 1 patient, bacterial endocarditis developed between the RCA and the right ventricle.

This group was divided for purposes of this review into two subsets: those 56 patients (60.22%) who had CAVFs

Table 3. Coronary Arteriovenous Fistulas: Sites of Origin and Drainage

	Drainage Site							
Origin	RV	PA	RA	LV	LA	CS	BV	Total
RCA	29	14	9	2	0	0	1	55
LAD	9	14	1	2	0	0	0	26
Circumflex	4	3	10	...	...	1	1	19
Diagonal	...	...	...	2	...	...	...	2
Obtuse marginal	...	...	...	...	...	1	...	1
LCA	...	...	1	...	...	...	...	1
Total	42	31	21	6	0	2	2	104

BV = bronchial vein; CS = coronary sinus; LA = left atrium; LAD = left anterior descending artery; LCA = left coronary artery; LV = left ventricle; PA = pulmonary artery; RA = right atrium; RCA = right coronary artery; RV = right ventricle.

alone and those 37 patients (39.78%) who had, in addition to a CAVF, an associated congenital or acquired cardiac lesion. Of the 56 patients diagnosed as having a CAVF alone, 41 (73.21%) were symptomatic. Sixty percent of the patients with symptoms reported angina, 34.14% reported dyspnea, and 26.83% reported palpitations (arrhythmias). Congestive cardiac failure was the presenting feature in 14.63% of patients with symptoms. Fifteen of the 56 were totally asymptomatic and were diagnosed only by virtue of a continuous murmur. All asymptomatic patients were less than 30 years of age.

Physical examination revealed the characteristic hallmark of a CAVF—the continuous machinery murmur, usually superficial in character, heard along the left sternal border in the second and third intercostal spaces. Twenty-one patients (37.50%) (including the 15 who were asymptomatic) had this characteristic murmur. In addition, a systolic murmur alone was heard in 6 patients and a diastolic murmur, in 4.

Thirty-six patients (64.29%) had ECG changes. The predominant ECG finding in these 36 was ischemia or chamber overload (66.67%). Infarction was experienced by only 4 patients (11.11%). Arrhythmias were present in 8 patients (22.22%), including ventricular premature contraction in 4 (11.11%), atrial tachyarrhythmias in 2 (5.56%), and conduction defects (bundle-branch block and first-degree atrioventricular block) in 2 (5.56%).

Chest roentgenographic examination revealed cardiomegaly in 38 patients (67.86%) (cardiothoracic ratios, 0.53 to 0.68). Twelve patients (16.50%) had radiologic evidence of a left-to-right shunt (pulmonary plethora).

Cardiac catheterization and angiography were done in all patients. Not only did these tests give accurate estimates of the left-to-right shunt, but they also gave the exact anatomic diagnosis—the location and the type of fistula. Oximetry measured left-to-right shunts (range, 1.36:1 to 2.3:1).

There were 37 patients with a CAVF who had an associated congenital or acquired cardiac lesion. Although coronary artery occlusive disease was the most frequent (in 35.14% of patients), no associated lesions occurred with sufficient frequency to establish a statistically significant relationship to CAVF. The patients in this category had predominantly symptoms and signs of the primary lesion; however, 8 patients also had a continuous low-pitched machinery murmur along the left sternal border.

Anomalies of Distribution

Ten patients were diagnosed as having an anomaly of distribution. These 6 male and 4 female patients ranged from 2 to 48 years in age. In 6 patients, the LCA system arose from the RCA, and in 4, the RCA system arose from the LCA. In 6 cases, there was an associated cardiac lesion. These included tetralogy of Fallot, ventricular septal defect and pulmonary stenosis with double-outlet right ventricle or with tricuspid regurgitation and mitral regurgitation, and mitral regurgitation alone.

The clinical presentation of this anomaly depends on two factors: any associated cardiac lesion and the presence or absence of atherosclerosis. Three patients complained of angina, and 4 patients appeared cyanotic. Tests found ECG changes suggestive of ischemia in 5 patients, arrhythmias in 3, and cardiomegaly in 4.

Surgical Techniques

Surgical treatment for coronary anomalies of origin was governed by the site of origin and coexisting cardiac lesions. On the 60 patients in whom coronary arteries originated in the PA, four basic surgical techniques were used: reimplantation (70% of patients), ligation and aortocoronary bypass (25%), ligation alone (3.33%), and the tunnel (Takeuchi) technique (1.67%). Fifty-six of these 60 had the LCA arising from the PA. Of the remaining 4, 2 had the RCA arising from the PA. In 1, reimplantation was used, but in the other, suspicion of ostial stenosis of the RCA made ligation with aortocoronary bypass using the saphenous vein the technique of choice. For the 2 patients in whom a branch of the LCA arose anomalously from the right PA, surgical correction of their associated lesions was also undertaken. In 1, surgeons corrected coexisting tetralogy of Fallot and ligated the anomalously arising left atrial branch. The other patient underwent aortic valve replacement to correct aortic stenosis, as well as reimplantation of the circumflex coronary artery into the aorta.

In the 18 patients in whom the LAD originated in the RCA, the anomalously arising LAD crossed the anterior aspect of the right ventricular outflow tract (RVOT), posing a problem in patching the RVOT for relief of infundibular pulmonic stenosis. To circumvent this limitation, surgeons mobilized the LAD artery and placed the outflow patch under the mobilized artery (44.44% of patients), used a right ventricle-to-PA conduit (38.89%), or ligated the anomalous artery and performed aortocoronary bypass to the distal LAD (16.67%). In this third method, surgeons used the saphenous vein in 2 patients and the left internal mammary artery in the third.

In the 10 patients in whom a coronary artery originated from the contralateral sinus of Valsalva, a combination of the four surgical methods was used. In 4 of the 6 patients whose RCA arose from the left sinus of Valsalva, surgeons excised the ostium of the RCA along with a cuff of aortic wall, then reimplanted it into the right anterior aortic wall. Care was taken to ensure that there was no angulation at the newly created ostium or in any part of the newly implanted vessel. Surgeons carefully closed the defect created in the aortic wall in the region of the left sinus of Valsalva with a patch of pericardium, making sure not to compromise the ostium of the LCA. In the 2 remaining patients, the RCA was ligated and aortocoronary bypass using saphenous vein was performed. Of the 4 patients whose circumflex coronary artery arose from the right sinus of Valsalva, 2 with ostial stenosis underwent aortocoronary bypass to the obtuse marginal branch of the circumflex, and the other 2 underwent ligation of the anomalous artery just distal to its origin at the right sinus of Valsalva and aortocoronary bypass to the obtuse marginal branch of the circumflex. The aim of the ligation was preventing competition of flow. In both cases, saphenous vein grafts were used.

Typically, CAVFs are surgically corrected; however, in cases in which associated cardiac lesions exist, a CAVF may be closed or left intact, depending on the physiologic significance of the shunt through the fistula, when the primary defect is corrected. The goal of surgical treatment is interruption of the fistulous tract—usually obliterating it totally—without compromise of normal coronary vessel flow. In this series, surgical treatment of the 104 CAVFs included internal closure (46.15% of fistulas), tangential arteriorrhaphy (28.85%), distal ligation alone (11.54%), proximal and distal ligation (6.73%), ligation and bypass grafting (3.85%), and closure from within a vessel dilated by an aneurysm (2.88%). Internal closure was used most frequently for fistulas that drained into a cardiac chamber, for fistulas whose identification on the surface of the heart was difficult, and for multiple fistulas. The second most frequently used technique, tangential arteriorrhaphy, was used for lateral fistulas. The fistula was first located by palpating for a thrill over the involved vessel. The fistula was then obliterated using multiple horizontal mattress sutures placed under the coronary artery. Complete obliteration was indicated by the disappearance of the thrill, reduction in the size of the recipient chamber, and failure of oximetry to show an oxygen saturation increase in the recipient chamber.

Of the 10 patients who had anomalies of distribution, 8 patients underwent operation. In 4 of these, surgeons corrected underlying cardiac lesions, as well as used a right ventricle-to-PA conduit to prevent trauma to the LAD crossing the anterior aspect of the RVOT. Three others, who were symptomatic and had ECG evidence of ischemia, underwent aortocoronary bypass grafting, including 2 who had an RCA system with the LCA running between the aorta and the PA. One patient underwent an aortocoronary bypass with mitral annuloplasty (No. 25 Duran ring). Surgeons used the internal mammary artery or bilateral mammary arteries. Operation was not recommended for 2 patients: 1 had multiple cardiac lesions and was in congestive cardiac failure, and the other was asymptomatic and scheduled for follow-up.

Table 4. Surgical Technique and Mortality for Treating Anomalous Origin of a Coronary Artery From the Pulmonary Artery

		Mortality (%)	
Technique	n	LCA	RCA
Reimplantation	42	2 (4.76)	0
Ligation and bypass	15	1 (6.67)	0
Ligation	2	1 (50.00)	0
Tunnel (Takeuchi)	1	0	0
Total	60	4 (6.67)	0

LCA = left coronary artery; RCA = right coronary artery.

Results

Of the 60 patients who underwent surgical treatment for a coronary artery arising anomalously from the PA, 4 (age range, 5 to 10 months) died in the immediate postoperative period (mortality, 6.60%) (Table 4). There were no delayed postoperative deaths. Two of the patients who underwent reimplantation and whose conditions were classified as being high risk died.

All patients had serial electrocardiograms on postoperative day 1, day 2, day 7, and just before discharge. Left ventricular function was assessed with echocardiography in the immediate postoperative period (within 24 hours) and just before discharge. Postoperative selective coronary angiography was not performed unless there was reason to believe that the patient still had myocardial ischemia or unless the patient was not progressing well postoperatively and it was thought that there was a possible mechanical reason (eg, kinking or torsion of the reimplanted artery or occlusion of a graft). Eighty-five percent had total relief from angina (symptomatically and on electrocardiograms) and improvement in left ventricular function (as assessed by echocardiography). In 3 patients (5%), cardiac failure persisted; in 5 patients (8.38%), postcardiotomy syndrome developed but responded to indomethacin and steroids. Two patients (3.33%) had residual ischemia, and in 1 patient (1.67%), a residual fistula persisted that required reoperation. One other patient (1.67%) had heart block. Of the 60 patients treated for this anomaly, 50 (83.33%) have been regularly followed up. Duration of follow-up ranges from 2 to 17 years.

In the 18 patients who underwent operation to correct an LAD originating in the RCA, there were two immediate postoperative deaths (11.11%). One of these patients was a 1-month-old girl who had had a right ventricle-to-PA conduit. She, in addition, had an anomalous retroesophageal subclavian artery, and her superior vena cava was on the left side. The other patient was a 5-year-old child who had undergone bypass with the left internal mammary to the distal LAD and could not be weaned from cardiopulmonary bypass. There were no delayed postoperative deaths. One patient had postcardiotomy syndrome that responded to antiinflammatory drugs. All patients have been regularly followed up, including 2 for 15 years. One patient has undergone reoperation for conduit stenosis and calcification.

In the 10 patients treated for origin of a coronary artery from the contralateral sinus of Valsalva, there were no immediate or delayed postoperative deaths. Regular follow-up was maintained with 8 patients. Follow-up ranges from 1 year to 12 years. One patient underwent reoperation for coronary artery occlusive disease.

In the group of 56 patients with CAVF only, there were no immediate or delayed deaths, and only 7.14% had complications. Two patients suffered myocardial infarction after proximal and distal ligation and had a stormy postoperative period, but survived. Another had a residual fistula that persisted after tangential arteriorrhaphy but underwent reoperation successfully. A 72-year-old woman had hemiparesis on the left side after closure of a CAVF on cardiopulmonary bypass; however, after 2 months, she was discharged from the hospital with minimal deficit. Of these 56 patients, only 6 (10.71%) were lost to follow-up.

In the group of 37 patients having a CAVF associated with other cardiac lesions, there were two postoperative deaths (5.41%), and 2 patients (5.41%) had complications after discharge from the hospital: one needed sternal debridement and rewiring for mediastinitis; the other required permanent pacemaker implantation to overcome persistent complete heart block. Unfortunately, follow-up has been possible only with 26 patients (70.27%), ranging from 10 months to 12 years.

In the 10 patients with anomalies of distribution, there were no postoperative in-hospital deaths. All 8 patients who underwent operation progressed well postoperatively, showing no evidence of residual ischemia. Five patients took a stress test 8 weeks after discharge from the hospital, and none had positive results. Follow-up, ranging from 1 year to 13 years, was maintained in 6 of the 10 patients. One patient, who had double-outlet right ventricle, ventricular septal defect, and pulmonary stenosis, had a reoperation for conduit stenosis.

Comment

Congenital anomalies of the coronary arteries form a rare but important subset of nonatherosclerotic coronary artery disease. Despite their rare occurrence (1% to 2% of the population) [1], these anomalies often are seen in patients in whom ischemic heart disease is uncommon and unsuspected. Moreover, they may occur along with and complicate other congenital heart defects, and as a result of abnormal course or distribution, increase the risk of coronary artery trauma during cardiac operations [2]. In addition, in most instances the natural history of these lesions is not associated with a normal life expectancy (with the exception of congenital origin of the RCA from the PA). Today, these anomalies can be easily diagnosed, accurately located, and safely corrected with gratifying long-term results, and for these reasons, surgical intervention should be strongly recommended once a precise diagnosis is established.

Anomalies of Origin

Origin of the LCA from the PA is rare, estimated to occur in 2.5% to 4.6% of patients with congenital cardiac anomalies. Though the anomaly was first reported by Brooks [4] in 1886, the clinical and hemodynamic syndrome was first described by Bland, White, and Garland [5] in 1933; hence, this anomaly is sometimes referred to as the Bland-White-Garland syndrome. In more than 90% of cases, it is the LCA that originates anomalously from the PA, generally from the left posterior sinus [2].

In this series, 56 of 60 (93.3%) cases involved the LCA arising from the PA; however, the RCA alone may arise from the PA (2 cases in this series), both coronary arteries may arise from the PA, or, rarely, a portion of the LCA system may arise from the PA (eg, the LAD or circumflex artery). Two such cases were found in this series. In 1, it was the circumflex branch, and in the other, it was the left atrial branch of the LCA that originated from the right PA. This anomaly, if left untreated, results in a high mortality, particularly in symptomatic infants. If the child survives infancy, a risk of sudden death still persists, inasmuch as 80% to 90% of those affected die suddenly by a mean age of 35 years. The pathophysiology of this syndrome was described by Edwards [6].

In a few cases, collateral circulation may develop fairly rapidly so that left ventricular myocardial perfusion is adequate. Myocardial ischemia and the later effects of fibrosis and mitral regurgitation do not occur then. Such patients survive and are seen later on in life with symptoms and signs proportional to the extent of intercoronary collaterals. In infants in whom adequate collateral circulation develops, a left-to-right shunt results, and blood flows from the RCA through the collaterals into the LCA and, thence, into the PA. It has been suggested that this may, in some cases, produce a sizable left-to-right shunt. However, in most cases of this adult-type syndrome, the shunt is of small volume and causes only a minimal hemodynamic effect on the left ventricle [6].

Patients with this syndrome have symptomatic angina. This results from either an inadequate RCA-to-LCA collateral flow or the "steal" phenomenon in which an adequate or excessive collateral flows into the low-pressure PA. Sudden and unexpected death is not an unusual result under these circumstances.

Anomalous origin of the RCA from the PA is a much rarer malformation, and the clinical manifestations of this condition are usually minimal or absent. Death is extremely rare. Nonetheless, this benign and rare anomaly can lead to myocardial ischemia, congestive heart failure, and myocardial fibrosis. Because it can be completely corrected once diagnosed, surgical correction is indicated. Origin of both coronary arteries from the PA has been reported but is extremely rare and fatal. In the reported cases, survival ranged from 9 hours to 5 months.

The goal of surgical therapy in anomalous origin of the LCA from the PA is to establish adequate left ventricular myocardial perfusion, and there appears little doubt that achieving anterograde flow of oxygenated blood into the LCA is the best treatment [7]. How the latter can be achieved is rather controversial, and several ingenious techniques have been described.

In the current series, reimplantation was performed in 75% of the patients with good results. There were only two postoperative deaths, and both of these patients had other cardiac lesions corrected simultaneously (left ventricular aneurysm repair, and ventricular septal defect and coarctation repair), greatly increasing their risk.

In cases in which reimplantation was not technically feasible from an anatomical standpoint (when the anomalous ostium was located anteriorly) [7], if the proximal LCA was aneurysmal, or if there existed membranous obstruction or ostial stenosis of the LAD or circumflex artery, surgeons resorted to ligation of the anomalous LCA with distal aortocoronary bypass using either the saphenous vein or the internal mammary artery. This technique was originally described by Cooley and coworkers [8] in 1966 and has the advantage of establishing a two-coronary artery system. The main disadvantage of this technique is the high rate of graft occlusion, especially in infants and children.

We, along with others [8], do not favor the use of simple ligation as a technique for correcting this anomaly because it can be safely used only if there exist adequate intercoronary collaterals. Also, it results in a one-coronary artery system, which poses a greater risk in the face of subsequent atherosclerosis. Furthermore, the incidence of sudden death has been found to be significantly higher in patients who have had ligation than in those who have a two-coronary artery system.

At the Texas Heart Institute, simple ligation, though used fairly frequently before 1966, was used in only 2 cases thereafter—one was an emergency ligation of the anomalous LCA in a neonate with intractable heart failure, and the other was a ligation of a left atrial branch that arose from the PA that was performed without any consequence.

Meyer and associates [9] in 1968 used the turned-down left subclavian artery and anastomosed it to the LCA. Though this is an ingenious idea, graft occlusion remains a major drawback. Moreover, there have been reports that the left subclavian artery has a tendency to kink at its origin. Experience at the Texas Heart Institute with this technique is very limited.

Finally, there is the novel tunnel technique described by Takeuchi and colleagues [10] in 1979. The advantages of this technique include establishing a two-coronary artery system, without mobilizing the LCA, and definite potential for growth with the in situ tissues that are used; the disadvantages are late complications of aortic incompetence and supravalvar pulmonic stenosis.

Although technically the anomaly of an LAD arising from the RCA is grouped under secondary anomalies [11], it has been considered and discussed here because of its frequent occurrence and because of its singularly important surgical implication. This anomaly is usually associated with other congenital heart defects, most commonly tetralogy of Fallot. (In this series, 15 of 18 patients [83.33%] had tetralogy of Fallot.) The LAD, after arising from the RCA, crosses over the anterior surface of the RVOT and eventually continues in its normal course. As a result of this abnormal course, the LAD is particularly vulnerable to injury when an incision is made in the right ventricle for relief and repair of RVOT obstruction. Injury to the LAD is an important cause of low-output syndrome after total correction of tetralogy of Fallot. Trauma to the LAD can be avoided by making a transverse or oblique ventriculotomy and fashioning it so as to avoid the LAD or by mobilizing the LAD and placing a transannular patch under it. Sometimes a right ventricle-to-PA conduit may be used. Rarely, the LAD is ligated and a distal aortocoronary bypass graft is done. It must be emphasized that surgeons must consider and treat each case on the basis of the existing anatomy and employ the most suitable technique.

When one coronary artery arises from the contralateral sinus of Valsalva, this vessel must traverse the base of the heart to reach its territory of distribution, passing anterior to, posterior to, or between the aorta and the right ventricular infundibulum. The importance of this seemingly benign anomaly is that it may result in sudden death, which usually occurs during or immediately after exercise. Such a tragic and fatal outcome is characteristic of the LCA arising from the right sinus of Valsalva [12].

The exact mechanism of sudden death is not clearly known, and several theories have been postulated. Benson and Lack [13] and Cohen and Shaw [14] initially postulated that the LCA was compressed between the aorta and PA as a result of an increase in cardiac output during exertion. This resulted in acute ischemia and ventricular fibrillation; however, it is difficult to comprehend how the low-pressure PA could compress a coronary artery whose pressure is systemic. Another hypothesis is that acute kinking disables a long left main artery and a congenitally small left coronary system [13]. The most reasonable explanation was proposed by Cheitlin, McAllister, and de Castro [15], who suggested that as the LCA arises from the right sinus of Valsalva, it forms an acute angle at its origin that may compromise its lumen as it passes anteriorly and leftward along the contour of the aorta posteriorly. Whatever the mechanism, this anomaly should always be suspected in young patients, particularly male patients with exertional chest pain or syncope [12].

We agree with other workers in recommending an immediate prophylactic bypass operation in all patients diagnosed as having the LCA arising from the right sinus of Valsalva. The high incidence of sudden death should support this approach [2, 12]. Because the patients are usually young, we prefer to use the mammary artery (one or both) for bypass grafting. On the other hand, in cases of the RCA arising from the left sinus of Valsalva, we advocate operation only if the patient is symptomatic, because angina—not sudden death—has been reported with this anomaly.

A special reference must be made regarding coronary anomalies associated with transposition of the great arteries. Variations in origin and branching of the coronary arteries in transposition have been well documented. Coronary anatomy must be thoroughly known before anatomic correction is undertaken. In almost all cases of transposition, the coronary arteries arise from one or both of the facing sinuses of the aorta [16]. Many ways of classifying these anomalies exist, but the system proposed by Yacoub and Radley-Smith [17] is the most useful from the surgical standpoint. Of importance are cases in which the coronary arteries take an intramural course. Intramural indicates an intimate relationship between the aortic and coronary artery walls [16]. Such coronary arteries are usually acutely angled at their origin; thus, excision of such an artery from the aortic wall and anastomosis to the pulmonary artery would cause kinking of the coronary artery. Hence, transferring an intramural coronary artery is not recommended [16].

Anomalies of Termination

Coronary arteriovenous fistula, first described by Krause [18] in 1865, constitutes the most common hemodynamically significant coronary artery anomaly [12, 13, 15]. It may be accurately defined as "a direct precapillary anastomosis between a major coronary artery and a cardiac chamber or major vessel (coronary sinus, superior vena cava, or pulmonary artery)" [2]. In this series, almost half of the total patients had this anomaly.

Although most commonly congenital in origin, this anomaly may also (but rarely) be acquired as a result of trauma. Recently, CAVFs have been reported in recipients of orthotopic heart transplants. These acquired fistulas usually involve the right ventricle and are thought to arise as a complication of endomyocardial biopsy. Anatomically, the RCA is the most frequent site of origin and the right ventricle, the most common recipient chamber. Bilateral fistulas (involving both coronary systems in the same patient) are reported in 4% to 5% of patients [19].

In this series also, the RCA was the most common site of origin (52.8%), and the right ventricle the most frequent recipient chamber (40.38%). Bilateral fistulas were seen in only 4 patients (4.3%). There were also 2 cases in this series in which the fistula drained into the bronchial veins. Fistulas draining into the left side are relatively rare (less than 10%) [19]. The age of the patient is very significant in identifying the anomaly [12]. Younger patients are generally asymptomatic. In this group, 15 patients were totally asymptomatic; all were less than 30 years of age.

Flow from the high-pressure artery into the low-pressure chamber or systemic vein occurs both during systole and diastole, producing the characteristic continuous murmur, and symptoms vary in magnitude directly in proportion to the size of the shunt.

Angina, in the absence of coronary artery disease (atherosclerosis), was the predominant symptom in this series and is thought to arise from an effect called "coronary steal," which produces ischemia by diverting blood from the high-resistance myocardial capillary bed into the low-resistance fistula [2]. The same phenomenon would precipitate angina if the flow in the involved vessel is borderline because of the presence of minimal occlusive disease, which does not show up on selective angiography. The relative incidence of symptoms in older patients could also be explained by the increased incidence of coronary occlusive disease with age and the long-term effects of volume overload [20]. In addition, CAVFs draining into the chambers on the right side may result in a left-to-right shunt, causing overload not only of the chambers, but also of the pulmonary circulation and the left ventricle.

Left untreated, CAVFs may result in several complications, and the incidence of complications increases with age [12]. Noteworthy are congestive cardiac failure, a common cause of death in untreated cases [11], bacterial endocarditis, and—though rare—mild to moderate pulmonary hypertension [21]. Finally, aneurysmal dilatation of the involved vessel and rupture of the fistula have been reported.

Although the surgical management of CAVFs has been controversial, now, with the knowledge of their complications and the ability to delineate them accurately, all hemodynamically significant CAVFs should be repaired whenever diagnosed [12, 22]. Correction in childhood constitutes optimal management and prevents the development of symptoms and complications [12]. The median sternotomy approach is the preferred surgical technique because it gives optimal exposure of the total coronary vascular tree. Moreover, it allows correction of other associated defects and permits the institution of cardiopulmonary bypass with ease.

Although many fistulas can be repaired without cardiopulmonary bypass, the Texas Heart Institute has used it during the last few years in almost all cases. The current approach is internal closure of the distal end of fistulas draining into the right ventricle or PA from within the recipient cavity. Localization can be improved immensely by releasing the cross-clamp or by infusing cardioplegia. For lateral fistulas, especially those on the surface of the right ventricle, tangential arteriorrhaphy (first described by Cooley and Ellis [20] in 1962) has been the technique of choice.

Proximal and distal ligation, a technique first described by Bjork and Crafoord [21] in 1947 and used extensively in the past, has been largely abandoned because of the risk of permanent myocardial ischemia or even infarction. Currently, this technique has been reserved for terminal fistulas from a main coronary trunk or those arising from secondary or accessory branches.

Finally, when the involved vessel has become aneurysmal, the vessel itself can be opened and the fistula closed from within. The arteriotomy can then be trimmed and repaired. It must be emphasized that the goal of surgical therapy should be complete obliteration of the fistulous tract with preservation of flow through the normal vessel.

Anomalies of Distribution

Having a single coronary artery is a very rare anomaly. Sharbaugh and White [23] found an incidence of 0.04%. Approximately 40% of patients with this anomaly have an associated congenital cardiac defect (eg, tetralogy of Fallot, transposition, or truncus arteriosus). Six of the 10 patients with this anomaly had associated congenital cardiac defects. There is no clear sex predominance in this condition, and the frequency of occurrence of single left and single right coronary arteries is approximately equal.

As in the case of anomalous origin from the contralateral sinus of Valsalva, one or more components of the coronary circulation must cross the base of the heart to reach the territory of distribution passing anterior to, posterior to, or between the great vessels. These transposed vessels may thereby be exposed to the risks of angulation or compression. On its own, this anomaly has been considered to be a benign anomaly because cardiac function is normal, provided all portions of the myocardium are perfused adequately; however, atherosclerosis is more prone to develop in the single coronary artery than in two normally arising arteries [6, 11]. When atherosclerosis develops, the consequences are severe because collateral circulation from a secondary coronary artery is not present. Because of this, occlusion of the proximal portion of a single coronary artery carries a grave prognosis.

The management of this anomaly alone is a problem. Some patients remain asymptomatic whereas some experience angina, infarction, or even sudden death. If the patient is severely symptomatic and no other associated disease is present to account for the symptoms, a bypass operation should be considered [2]. If the patient has mild symptoms but no atherosclerosis, then additional tests for myocardial ischemia may be helpful: atrial pacing with lactate metabolism determination, maximal treadmill exercise, or thallium stress testing. If test results are abnormal, then conventional therapy for ischemia should be advised, and the patient should be scheduled for close follow-up.

Conclusion

It must be reemphasized that the major anomalies and some of the clinically significant minor anomalies are all associated with a reduced life expectancy and even sudden death. It is imperative that they are diagnosed early and treated appropriately. A high index of suspicion, in a physician evaluating a young individual thought to have coronary artery disease, is the cornerstone for a successful outcome.

As highlighted earlier, anomalous origin of the LCA from the PA is a very important cause of ventricular dysfunction, intractable cardiopulmonary failure, and even death in infants. Infants with this anomaly require immediate intervention. It is always preferable to establish an anterograde flow of oxygenated blood through the coronary arteries and to maintain a two-coronary artery system. Reimplantation of the anomalous LCA into the aorta achieves both these objectives. In cases in which this was not possible in this series, good results were obtained with ligation of the anomalous vessel with distal aortocoronary bypass.

Coronary arteriovenous fistula was the most common anomaly in this series. It can be confused with many other congenital cardiac defects (patent ductus arteriosus, ventricular septal defect with prolapse of aortic cusp, or aorticopulmonary window); therefore, it is important to establish a correct diagnosis and accurately localize the fistula. This review revealed that young patients are usually asymptomatic, and the severity of the symptoms is proportional to the size of the shunt. In addition to chamber overload, resulting from the left-to-right shunt, CAVFs also produce angina by the phenomenon of "coronary steal." Tangential arteriorrhaphy and internal closure of the fistulas are efficient techniques because they not only totally obliterate the fistula, but also preserve anterograde flow through the normal vessel. A median sternotomy for exposure and the use of cardiopulmonary bypass is preferred in all cases. Finally, three anomalies previously considered insignificant—namely, origin of a coronary artery from the contralateral sinus of Valsalva, LAD arising from the RCA, and a single coronary artery—have now gained immense importance because they offer an explanation for sudden death in young individuals (especially a single coronary artery or a coronary artery originating from the contralateral sinus of Valsalva) and predispose the coronary arteries to surgical trauma during repair of other congenital defects affecting the blood's course and distribution. For these reasons, adequate knowledge of these anomalies and their accurate demonstration by cineangiography are essential in avoiding catastrophic outcomes.

References

1. Engel HJ, Torres C, Page L Jr. Major variations in anatomical origin of the coronary arteries: angiographic observations in 4,250 patients without associated congenital heart disease. Cathet Cardiovasc Diagn 1975;1:157–69.
2. Levin DC, Fellows KE, Abrams HL. Hemodynamically significant primary anomalies of the coronary arteries: angiographic aspects. Circulation 1978;58:25–34.
3. Augustsson MH, Gasul BM, Fell EH, et al. Anomalous origin of left coronary artery from pulmonary artery: diagnosis and treatment of infantile and adult types. JAMA 1962;180:15–21.
4. Brooks HStJ. Two cases of an abnormal coronary artery of the heart arising from the pulmonary artery with some remarks upon the effect of this anomaly in producing cirsoid dilation of the vessels. J Anat Physiol 1886;20:26–9.
5. Bland EF, White PD, Garland J. Congenital anomalies of the coronary arteries: report of an unusual case associated with cardiac hypertrophy. Am Heart J 1933;8:787–801.
6. Edwards JE. Symposium on cardiovascular diseases: functional pathology of congenital cardiac disease. Pediatr Clin North Am 1954;1:13–49.
7. Laborde F, Marchand M, Leca F, Jarreau M-M, Dequirot A, Hazan E. Surgical treatment of anomalous origin of the left coronary artery in infancy and childhood: early and late results in 20 consecutive cases. J Thorac Cardiovasc Surg 1981;82:423–8.
8. Cooley DA, Hallman GL, Bloodwell RD. Definitive surgical treatment of anomalous origin of left coronary artery from pulmonary artery: indications and results. J Thorac Cardiovasc Surg 1966;52:798–808.
9. Meyer BW, Stefanik MD, Stiles QR, Lindesmith GG, Jones JC. A method of definitive surgical treatment of anomalous origin of left coronary artery. J Thorac Cardiovasc Surg 1968;56:104–7.
10. Takeuchi S, Imamura H, Katsumoto K, et al. New surgical method for repair of anomalous left coronary artery from pulmonary artery. J Thorac Cardiovasc Surg 1979;78:7–11.
11. Ogden JA. Congenital anomalies of the coronary arteries. Am J Cardiol 1970;25:474–9.
12. Liberthson RR, Sagar K, Berkoben JP, Weintraub RM, Levine FH. Congenital coronary arteriovenous fistula: report of 13 patients, review of literature and delineation of management. Circulation 1979;59:849–54.

13. Benson PA, Lack AR. Anomalous aortic origin of left coronary artery: report of two cases. Arch Pathol 1968;86:214–6.
14. Cohen LS, Shaw LD. Fatal myocardial infarction in an 11 year old boy associated with a unique coronary artery anomaly. Am J Cardiol 1967;19:420–3.
15. Cheitlin MD, McAllister HA, de Castro CM. Myocardial infarction without atherosclerosis. JAMA 1975;231:951–9.
16. Gittenberger de Groot A, Sauer U, Quaegbeur J. Aortic intramural coronary artery in three hearts with transposition of great arteries. J Thorac Cardiovasc Surg 1986;91:566–71.
17. Yacoub M, Radley-Smith R. Anomalies of the coronary arteries in transposition of the great arteries and methods of their transfer in anatomical correction. Thorax 1978;33:418–20.
18. Krause W. Ueber den Ursprung einer access orischen a. coronaria cordis aus der a. pulmonalis. Z Rat Med 1865;24:225–7.
19. Liotta D, Hallman GL, Hall RJ, Cooley DA. Surgical treatment of congenital coronary artery fistula. Surgery 1971;70:856–64.
20. Cooley DA, Ellis PR. Surgical considerations of coronary arterial fistula. Am J Cardiol 1962;10:467–74.
21. Bjork G, Crafoord C. Arteriovenous aneurysm in the pulmonary artery simulative patent ductus arteriosus Botalli. Thorax 1947;2:65–70.
22. Hudspeth AS, Linder JH. Congenital coronary arteriovenous fistula. Arch Surg 1968;96:832–8.
23. Sharbaugh AH, White RS. Single coronary artery: analysis of the anatomic variation, clinical importance, and report of five cases. JAMA 1974;230:243–6.

Notice From the Southern Thoracic Surgical Association

The Thirty-ninth Annual Meeting of the Southern Thoracic Surgical Association will be held at the Saddlebrook Golf and Tennis Resort, Wesley Chapel (near Tampa), Florida, November 5–7, 1992. Members may register upon payment of a $50 fee. There will be a $300 registration fee for nonmember physicians except for guest speakers, speakers on the program, and residents. There will be a $50 registration fee for attendees of the Postgraduate Course, which will be held the morning of Thursday, November 5, 1992. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected primarily as a means to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Advance registration forms, hotel reservation cards, and details regarding transportation arrangements have been mailed to Association members. Nonmembers should write to the Secretary-Treasurer, Hendrick B. Barner, MD.

Hendrick B. Barner, MD
Secretary-Treasurer
Southern Thoracic Surgical Association
401 North Michigan Avenue
Chicago, IL 60611-4267
(312) 644-6610

Exocrine Pancreatic Function in Mediastinal Teratomata: An Aid to Preoperative Diagnosis?

Panny Kallis, FRCS, Tom Treasure, FRCS, S. J. Keith Holmes, FRCS, and Meryl Griffiths, MRCPath

Cardiothoracic Surgery, St. George's Hospital, London, England

The diagnosis of teratoma may be made by demonstration of high amylase content in fluid aspirated from anterior mediastinal lesions. In 2 cases of mediastinal teratoma proteolytic enzyme activity was evident at the time of operation. A diagnosis of mediastinal teratoma was aided in 2 subsequent cases by demonstration of elevated amylase activity in the aspirated fluid before definitive operation.

(Ann Thorac Surg 1992;54:741–3)

Teratoma is one of the more common mediastinal tumors [1], and the occurrence of pancreatic tissue in mediastinal teratomata is well documented [2]. Isolated cases of benign mediastinal teratomata exhibiting pancreatic endocrine [3] or exocrine secretion [4] have been reported.

We report 4 cases of mediastinal teratomata with evidence of exocrine pancreatic activity. Two had evidence of severe inflammation and erosion of surrounding structures, including florid pericarditis, due to pancreatic enzyme activity. Preoperative aspiration had not been attempted but subsequent histologic examination revealed well-differentiated pancreatic tissue. In 2 subsequent cases the diagnosis was suggested, by demonstration of elevated amylase activity in the aspirated fluid at the time of assessment, before definitive operation.

This suggests the possibility of preoperative needle aspiration of anterior mediastinal tumors for pancreatic enzyme estimation as a means of establishing the diagnosis.

Case Reports

Patient 1

A 17-year-old boy had a 9-month history of lower chest pain relieved by sitting forward, shortness of breath, night sweats, and weight loss. An electrocardiogram (Fig 1) revealed pericardial changes and an anterior mediastinal mass was confirmed by a chest roentgenogram and computed tomographic scan. Pericardiocentesis produced 400 mL of serosanguineous fluid which showed no evidence of malignancy or bacterial growth, but amylase estimation was not considered at the time. With a working diagnosis of a malignant tumor invading the pericardium the mass was explored through a median sternotomy. There was generalized inflammation, and apparent abscess formation turned out to be sebaceous material. The diagnosis of dermoid was made when a frozen section demonstrated squamous epithelium, and the mass was completely removed with the anterior pericardium. Histologic examination confirmed benign cystic teratoma including exocrine pancreatic tissue and islets of Langerhans (Fig 2) as well as skin, smooth muscle, respiratory epithelium, and gastrointestinal mucosa. Two years later he remains alive and well.

Patient 2

A 24-year-old man had a 1-week history consistent with pericarditis, which was confirmed with an electrocardiogram. A chest roentgenogram and computed tomographic scan revealed an anterior mediastinal mass extending to the left side. At median sternotomy the inflammatory mass and the involved pericardium were removed. He made an uneventful recovery, and histologic examination confirmed a benign teratoma containing pancreatic tissue with islets of Langerhans as well as gastric, squamous, and respiratory epithelium. The patient remains alive and well a year later.

Patient 3

An 8-year-old girl had a 2-month history of right-sided pleuritic chest pain and increasing shortness of breath. A chest roentgenogram (Fig 3) revealed a mediastinal mass, which was confirmed by magnetic resonance imaging (Fig 4). After progression of her symptoms she was admitted on an emergency basis and an urgent tissue diagnosis was requested by the pediatric oncologist managing the case. A right anterior mediastinotomy was performed through the second intercostal space. Experience with the previous 2 cases led the operating surgeon to aspirate the lesion, which produced dark brown fluid containing an amylase level of 2,608 IU/L and no malignant cells. With an established diagnosis of cystic teratoma she underwent a median sternotomy and excision of the tumor within a week. She made an uneventful recovery, and histologic examination confirmed a benign cystic teratoma containing pancreatic tissue, gastrointestinal epithelium, squamous epithelium, sebaceous glands, and smooth muscle. A year later the patient remains alive and well.

Patient 4

A 4-year-old boy had a 4-day history of increasing dyspnea and a bulging deformity of the left side of his chest. On examination he was in respiratory distress with tachy-

---

Accepted for publication Feb 20, 1992.

Address reprint requests to Dr Kallis, Department of Cardiothoracic Surgery, St. George's Hospital, London SW17 0QT, England.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

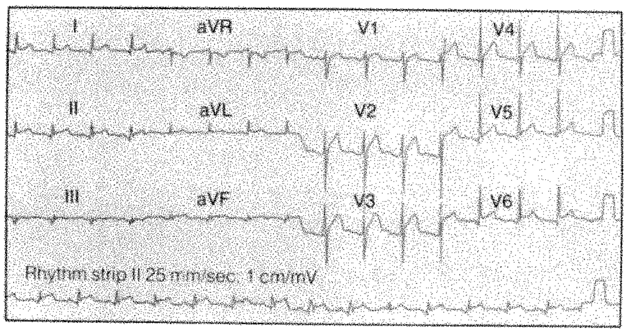


Fig 1. Electrocardiogram showing ST segment elevation consistent with pericarditis.

pnea and a bulging asymmetry of his left anterior chest wall. A chest roentgenogram showed a large mediastinal mass with compression of the trachea and main bronchi. Multiple bilateral lung metastases were also noted and confirmed by a computed tomographic scan. All tested tumor markers were negative (vanillylmandelic acid, catecholamines, human chorionic gonadotropin, α-fetoprotein). With a working diagnosis of soft tissue sarcoma or malignant teratoma producing critical major airway ob-

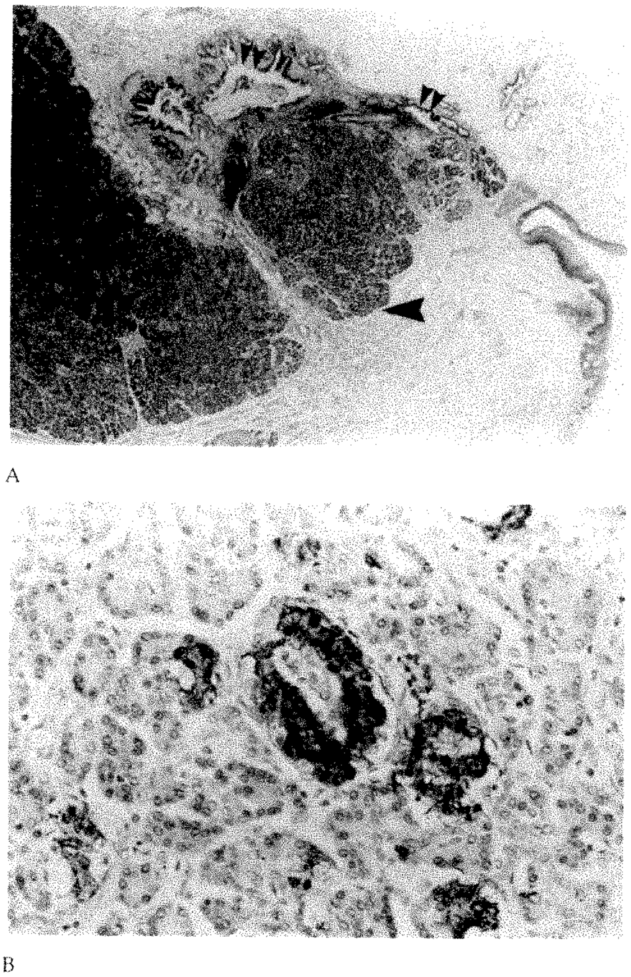


Fig 2. (A) A section from the wall of the cyst showing pancreatic tissue (arrow) *complete with a pancreatic duct* (double arrow), *apparently opening into the cavity of the cyst, which is lined by squamous epithelium and intestinal mucosa. (Hematoxylin and eosin, ×25 before 38% reduction.) (B) Pancreatic tissue stained to demonstrate insulin-producing islets of Langerhans* (darkly stained), *which are surrounded by exocrine pancreatic acini. (Immunoperoxidase preparation using antiinsulin antibody.)*

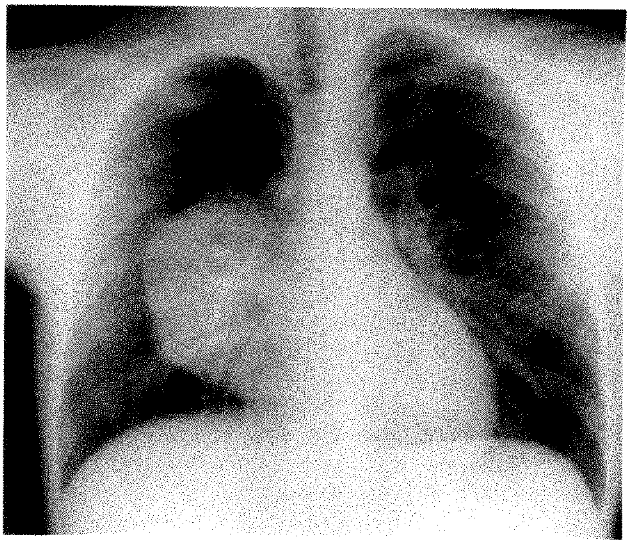


Fig 3. Chest roentgenogram showing a large mediastinal mass extending to the right side.

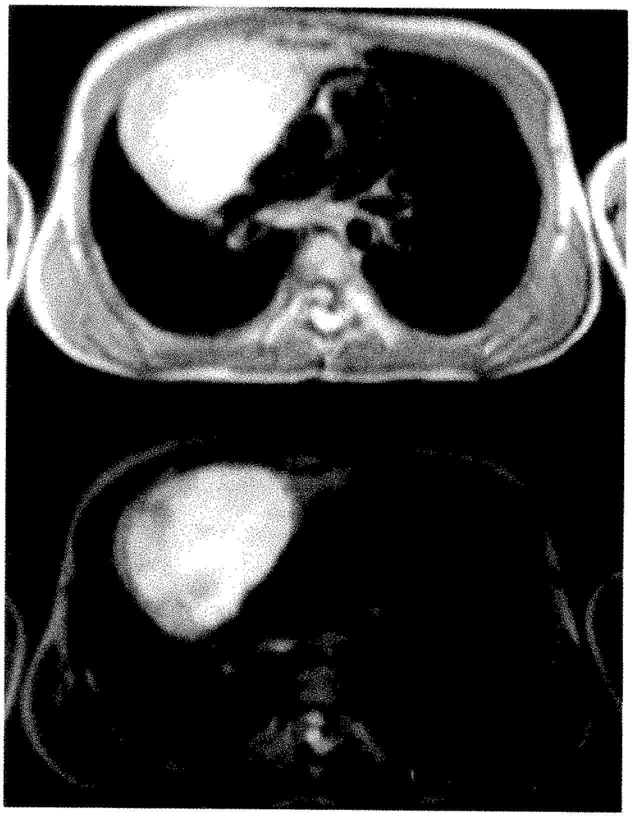


Fig 4. Magnetic resonance image showing a large mediastinal mass in close relation to the great vessels and extending toward the right pleural cavity.

struction, based on the opinion of the pediatric oncologist managing the case, chemotherapy was started (carboplatin, epirubicin, and vincristine). Biopsy of the mass was performed 3 days later through a left anterior mediastinotomy. The mass consisted of multiple irregular nodules and cysts containing dark green fluid (amylase level >3000 IU/L). Histologic examination revealed exocrine glandular tissue as well as other tissues consistent with a teratoma, but no evidence of malignancy was seen. The patient made a rapid recovery and was discharged home 2 days later.

The patient received six courses of chemotherapy during the following 3 months with a reduction in the size of the mediastinal mass and the secondary nodules as assessed by a computed tomographic scan of the thorax. Subsequently the mass and several residual pulmonary nodules were resected through a transverse thoracotomy. Histologic examination revealed differentiated teratoma, with three minute foci of partly differentiated rhabdomyosarcoma, classified as malignant teratoma intermediate. During the last follow-up, 2 months after resection, the patient was asymptomatic but further lung metastases were noted on routine chest roentgenogram.

Comment

Examples of constituent tissues of teratomata performing their normal physiological function include hair and tooth growth, sebaceous secretion, secretion of insulin, secretion of amylase, and production of thyroxine (ovarian teratoma).

About half of the cases of mediastinal teratomata from three reported series [2, 5, 6] contained pancreatic tissue. Schlumberger [5] demonstrated the presence of pancreatic tissue in 8 of 16 cases, and Inada and Nakamo [6] in 6 of 15 cases of mediastinal teratomata. Suda and colleagues [2] found that 11 of their 19 cases contained well-differentiated pancreatic tissue. Most of the pancreatic tissue contained islets of Langerhans, most of which contained beta-cell granules as in normal pancreatic tissue. Alpha and delta granules, however, were demonstrated in fewer islets than those in normal pancreatic tissue. In the exocrine portion of the specimens, zymogen granules were found in the acinar tissues as in normal pancreatic tissue. These authors concluded that the pancreatic tissue observed in teratomata is morphologically and functionally similar to normal pancreatic tissue. By contrast, no pancreatic tissue was found in 353 cases of ovarian teratomata and in 80 cases of testicular teratomata [2].

Sommerlad and associates [7] and Southgate and Slade [4] reported 2 cases of benign mediastinal teratomata in which they detected high amylase activity in the cystic fluid. Hiraiwa and co-workers [8] reported a case of benign mediastinal teratoma that ruptured into the pleural cavity. The pleural fluid contained 116 IU/L of amylase and the cystic fluid 813 IU/L of amylase. Microscopic examination and immunoperoxidase staining, however, revealed that the amylase was produced by acinar cells resembling salivary gland.

Hodes and colleagues [9] were only able to demonstrate immunoreactive amylase in 2 of 9 cases of pancreatic tissue in sacrococcygeal teratomata.

Erosion of mediastinal teratomata into adjacent structures is well documented. Galy and associates [10] reported 3 cases of fistula into the bronchial tree. Marsten and co-workers [11] described a case of acute cardiac tamponade due to perforation into the pericardial sac.

Endocrine function of pancreatic tissue in teratomata has also been documented. Honicky and colleagues [3] reported a case of benign mediastinal teratoma producing insulin that resulted in hypoglycemia.

The common feature of all 4 of our patients is the presence of exocrine pancreatic function leading to inflammation of the surrounding structures. An aggressive tumor forms part of the differential diagnosis because of the short history of presentation, which may be the result of the inflammation produced by the pancreatic enzymes. Based on the experience in the first 2 patients a diagnosis of cystic teratoma was made by demonstrating elevated amylase level in the aspirated fluid in the subsequent 2 patients before definitive operation.

The most common anterior mediastinal masses are thymoma, teratoma, lymphoma, intrathoracic thyroid, and bronchogenic cysts. On the basis of this experience we will send an aliquot of fluid aspirated from these lesions for estimation of amylase activity as a matter of clinical routine. Apart from lymphoma, surgical excision is the management of choice. A needle aspiration for the detection of pancreatic enzymes leading to a preoperative diagnosis of a mediastinal teratoma would permit exploration and excision at one stage.

References

1. Rubush JL, Gardner IR, Boyd WC, Ehrenhaft JL. Mediastinal tumors. Review of 186 cases. J Thorac Cardiovasc Surg 1973;65:216–22.
2. Suda K, Mizuguchi K, Hebisawa A, Wakabayashi T, Saito S. Pancreatic tissue in teratoma. Arch Pathol Lab Med 1984;108: 835–7.
3. Honicky RE, dePapp EW, Rochester NY. Mediastinal teratoma with endocrine function. Am J Dis Child 1973;126: 650–3.
4. Southgate J, Slade PR. Teratodermoid cyst of the mediastinum with pancreatic enzyme secretion. Thorax 1982;37: 476–7.
5. Schlumberger HG. Teratoma of anterior mediastinum in the group of military age: a study of 16 cases, and a review of theories of genesis. Arch Pathol Lab Med 1946;41:398–444.
6. Inada K, Nakano A. Structure and genesis of the mediastinal teratoma. Kyobu Geka 1961;11:211–8.
7. Sommerlad BC, Cleland WP, Yong NK. Physiological activity in mediastinal teratomata. Thorax 1975;30:510–5.
8. Hiraiwa T, Hayashi T, Kaneda M, et al. Rupture of a benign mediastinal teratoma into the right pleural cavity. Ann Thorac Surg 1991;51:110–2.
9. Hodes JE, Hull MT, Mirkin LD, Hodes ME. Immunohistochemical demonstration of altered functional differentiation of pancreatic tissue in sacrococcygeal teratomas. Hum Pathol 1983;14:724–6.
10. Galy P, Brune J, Dorsit G, Russet H, Seigneuric A, Porte J. Trois cas de kystes dermoides du mediastin fistulisés dans les bronches. Lyon Médical 1971;226:389–91.
11. Marsten JL, Cooper AG, Ankeney JL. Acute cardiac tamponade due to perforation of a benign mediastinal teratoma into the pericardial sac. J Thorac Cardiovasc Surg 1966;51:700–7.

Endotoxin Release and Tumor Necrosis Factor Formation During Cardiopulmonary Bypass

Nicolaas J. G. Jansen, MD, PhD, Willem van Oeveren, PhD, Y. J. Gu, MD,
Marilijn H. van Vliet, MD, Leon Eijsman, MD, PhD, and
Charles R. H. Wildevuur, MD, PhD

Department of Cardiopulmonary Surgery Research Division, University Hospital Groningen, The Netherlands, and Department of Anesthesiology and Cardio-Pulmonary Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

Endotoxin, when released into the systemic circulation during cardiopulmonary bypass (CPB), might induce activation of plasmatic systems and blood cells during CPB, in addition to a material-dependent blood activation during CPB. However, the role of endotoxin in the development of this so-called whole-body inflammatory reaction in CPB is still unclear. We investigated the release of endotoxin into the systemic circulation in relation with the activation of the complement system and in particular the formation of tumor necrosis factor in 10 patients undergoing CPB. Immediately after the start of CPB the endotoxin concentrations increased significantly ($p < 0.01$), accompanied by increases in C3a concentration ($p < 0.05$). After release of the aortic cross-clamp, there was a second increase in endotoxin followed by a continuous increase in tumor necrosis factor, reaching a peak concentration 1 hour after the end of CPB ($p < 0.01$). These observations demonstrate a release of endotoxin into the systemic circulation associated with tumor necrosis factor formation, which contributes to the whole-body inflammatory reaction associated with CPB.

(Ann Thorac Surg 1992;54:744–8)

Patients undergoing cardiopulmonary bypass (CPB) are at risk for development of a postperfusion syndrome. In its most pronounced form this consists of pulmonary and renal dysfunction and hemodynamic instability in the postoperative period [1]. These events are considered to be caused by the whole-body inflammatory reaction due to extensive blood activation by the material of the extracorporeal circuit [2]. The activation of the complement system is one of the major pathways leading to the whole body inflammatory reaction, by activation of polymorphonuclear leukocytes [3]. The activation of plasmatic systems and blood cells leading to the whole-body inflammatory reaction resembles the activation by endotoxin in gram-negative sepsis [4, 5]. Recent studies showed that endotoxin can be present during CPB [6, 7].

Tumor necrosis factor (TNF) is released in response to endotoxin and gram-negative bacterial products and is considered to be the prime mediator involved in the pathophysiology of gram-negative sepsis [8, 9]. In a recent study we showed that formation of TNF during CPB is correlated with the clinical hemodynamic instability after CPB [10]. It might therefore be assumed that endotoxin, when it is released into the systemic circulation, could play an important role in the whole-body inflammatory reaction, especially when this is accompanied by TNF formation. In a prospective study we investigated 10 patients undergoing CPB and measured endotoxin, complement activation, and TNF concentrations during and immediately after CPB.

Patients and Methods

Ten patients undergoing elective primary coronary artery bypass grafting procedures were studied. All patients gave their informed consent. Patients with insulin-dependent diabetes mellitus, preoperative use of corticosteroids, or chronic obstructive disease were not included. The average age of the patients (± standard error of the mean) was 63 ± 2 years. They had an average body surface area of 1.9 ± 0.1 m^2 and a mean body weight of 72 ± 3 kg. These patients were in bypass for 109 ± 10 minutes and had an average cross-clamp time of 66 ± 7 minutes.

The extracorporeal circuit consisted of a Bard hollow fiber membrane oxygenator (Model HF 4000, Bard Inc, William Harvey, Santa Ana, CA), a Bard cardiotomy reservoir with filter (Model H-705 F), and a Bard arterial line filter (Model H-625). Polyvinyl chloride tubing was used except for the pump tubing, which was silicon rubber. The extracorporeal circuit was primed with 2.2 L of Ringer's lactate, 0.2 L of 20% human albumin (CLB, Amsterdam, The Netherlands), and 50 mg of heparin (Leo, Emmen, The Netherlands).

Heparin (300 IU/kg) was given intravenously before cannulation of the aorta, and this was repeated in a dosage of 25 mg whenever the activated clotting time was shorter than 400 seconds. Heparin was neutralized by an intravenous injection of 300 IU of protamine sulfate within 5 minutes after the end of perfusion. A nonpulsa-

---

Accepted for publication Feb 21, 1992.

Dr Jansen's present address is Department of Pediatrics, University Hospital, Maastricht, The Netherlands.

Address reprint requests to Dr van Oeveren, Department of Cardiopulmonary Surgery Research Division, University Hospital, Oostersingel 59, 9713 EZ Groningen, The Netherlands.

© 1992 by The Society of Thoracic Surgeons

tile flow of 2.0 to 2.4 L/m^2 · min was used at a moderate hypothermia of 28° to 30°C.

When the distal coronary artery anastomosis was established, the aorta was cross-clamped and cardioplegia was achieved with a 0°C isotonic solution containing 15 mmol/L K^+, 15 mmol/L Mg^{2+} and 1.5 g/L procaine hydrochloride. Cardioplegia was repeated every 20 minutes. An average of about 2 L cardioplegic fluid was used.

Anesthetic Technique

Anesthesia was started with a bolus of alfentanil (50 μg · kg^{-1} · min^{-1}) and etomidate (0.1 mg/kg) followed by pancuronium bromide (0.1 mg/kg). At termination of CPB inotropic drugs were given if necessary. All patients were ventilated to normocapnia (carbon dioxide tension, 4.5 to 5.0 kPa) with 50% oxygen in air.

Hematology

Blood samples were taken from the radial artery or arterial line of the extracorporeal circuit after induction of anesthesia, 5 minutes before CPB, 5 and 30 minutes after the start of CPB, at the end of CPB, and 30 minutes after protamine sulfate administration. In addition, blood was collected 5 minutes before and 5 minutes after release of the aortic cross-clamp.

Two milliliters of blood, anticoagulated with 0.318% citrate, was collected sterile and put in pyrogen-free tubes for determination of the endotoxin concentration. After collection blood was centrifuged at low speed (100 *g*) to obtain platelet-rich plasma, which was stored in pyrogen-free tubes. All further procedures were done aseptic to exclude contamination; only pyrogen-free tubes and reagent waters were used.

In this platelet-rich plasma the endotoxin concentration was measured by activation of a proenzyme present in limulus amoebocyte lysate (Coatest-Endotoxin; Kabivitrum Diagnostica, Stockholm, Sweden) and by conversion of the substrate S 2423, which was measured in a spectrophotometer (Uvikon 710; Kontrom, Zurich, Switzerland) at 405 nm [11].

Three milliliters of blood, anticoagulated with EDTA (0.01 mol/L), was centrifuged and stored at −70°C for C3a assays. C3a des arg concentrations were determined by radioimmunoassay (Upjohn Co, Kalamazoo, MI).

One milliliter of blood, anticoagulated with EDTA (0.01 mol/L), was used for determination of TNF using a radioimmunoassay (TNFa IRMA; Medgenix, Brussels, Belgium). This assay is based on oligoclonal antibodies against different epitopes of TNFa, which are bound to the tubes, and subsequent binding of iodine-labeled antibodies to the bound TNFa. Plasma samples and antibodies are simultaneously incubated for 18 to 20 hours, which renders a high sensitivity of the assay.

Statistics

A repeated-measures analysis of variance (StatView Software; Brainpower Inc, Calabasas, CA) was performed to inspect the differences among different sampling points. Significant differences between the specific time points were determined by the paired Student's *t* test. The data are presented as means ± standard error of the mean. A *p* value less than 0.05 was considered to be significant.

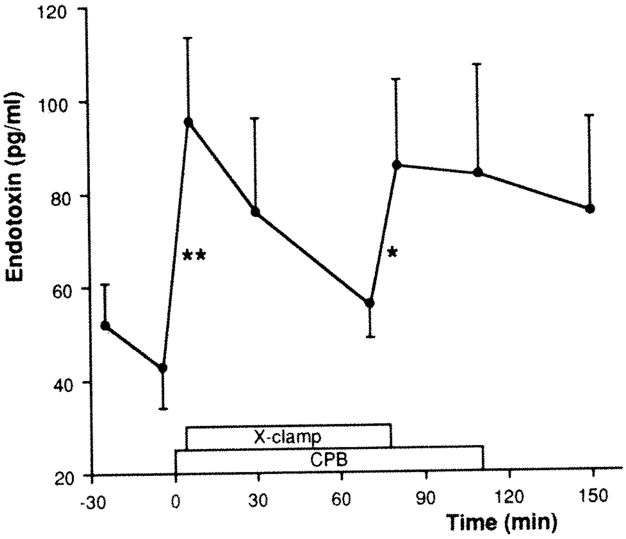


*Fig 1. Endotoxin concentration in platelet-rich plasma during and after cardiopulmonary bypass (CPB). Immediately after the start of CPB there is a significant increase in endotoxin concentration (**$p <$ 0.01 versus 5 minutes before the start of CPB), with a second significant increase 5 minutes after release of the aortic cross-clamp (X-clamp). (*$p <$ 0.05 versus 5 minutes before the clamp release.)*

Results

Endotoxin

At induction of anesthesia endotoxin was detectable, reaching lower concentrations before the start of CPB. Immediately after the start of CPB a significant increase in endotoxin was observed ($p < 0.01$), after which the concentrations decreased. After release of the aortic cross-clamp a second significant increase of endotoxin was observed ($p < 0.05$), and thereafter the endotoxin concentration remained elevated until 30 minutes after protamine administration (Fig 1).

Complement Activation

After the start of CPB the C3a concentration increased significantly ($p < 0.05$). Upon release of the cross-clamp a second, not statistically significant, increase was seen, with a maximum of 2,268 ng/mL and a range of 1,040 to 4,400 ng/mL. Thereafter the C3a concentration decreased and remained stable until 30 minutes after protamine administration (Fig 2).

Tumor Necrosis Factor

Tumor necrosis factor could be measured after release of the cross-clamp and increased significantly to a maximum of 11 pg/mL, with a range of 4 to 27 pg/mL, at 30 minutes after protamine administration ($p < 0.01$) (Fig 3).

Comment

The endotoxin concentration increased significantly 5 minutes after the start of CPB and after release of the aortic cross-clamp and remained elevated thereafter. The high level of endotoxin seen after induction of anesthesia and after the start of bypass could be due to pyrogens present in the fluids administered to the patients and to endotoxin contamination of the perfusion circuit, the cardiac suction lines, and cardioplegic fluids [7]. It has been discussed that this kind of "environmental" endotoxins are less pathogenic than endotoxin derived from gram-negative bacteria [12]. At least all patients were in good clinical condition before operation, and all blood cultures taken intraoperatively were negative.

The increase in endotoxin after release of the aortic cross-clamp might be explained by the preceding hypoperfusion of the splachnic bed by the reduced peak arterial pressure associated with the nonpulsatile flow of the pump during CPB [6]. This hypoperfusion leads to an injury of the mucosal barrier between the gut and blood vessel wall [13], and large quantities of endotoxin may enter the portal vein [14]. Endotoxin, in turn, promotes bacterial translocation, a process in which bacteria, normally confined to the gut, will cross the intestinal mucosal barrier and appear in the mesenteric lymph nodes and other systemic organs [15, 16]. Endotoxins, passing the mucosal barrier of the gut either by hypoperfusion or by translocation, can reach the portal or the lymph circulation. Under normal conditions a systemic endotoxemia is prevented by removal of endotoxin by the Kupffer cells of the liver [17]. However, during CPB the Kupffer cell function can be suppressed by an overloading of the reticuloendothelial cells by cellular debris and aggregated proteins, and so a variable amount of endotoxin can enter the systemic circulation [6, 18]. The decrease in endotoxin concentration seen in the initial period of CPB suggests that clearance still occurs at that time. After release of the cross-clamp, however, the heart is allowed to eject normally again, which will increase the flow through the splachnic bed and could flush out more endotoxin into the portal circulation, which might explain the increase in endotoxin on release of the cross-clamp. Due to the impaired function of the Kupffer cells the concentration of endotoxin remains high afterward and can lead to ongoing activation [7].

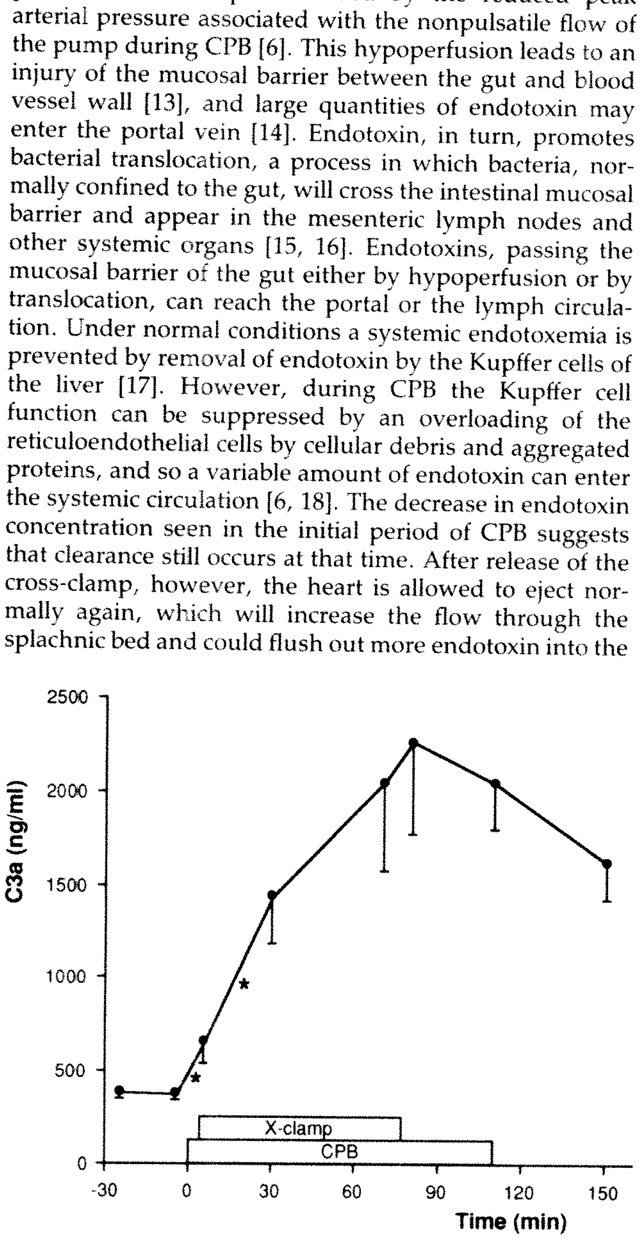


*Fig 2. Complement C3a concentration in plasma during and after cardiopulmonary bypass (CPB). C3a concentration increased steadily after start of CPB, with a second small increase after release of the aortic cross-clamp (X-clamp). (*p < 0.05 versus 5 minutes before the start of CPB.)*

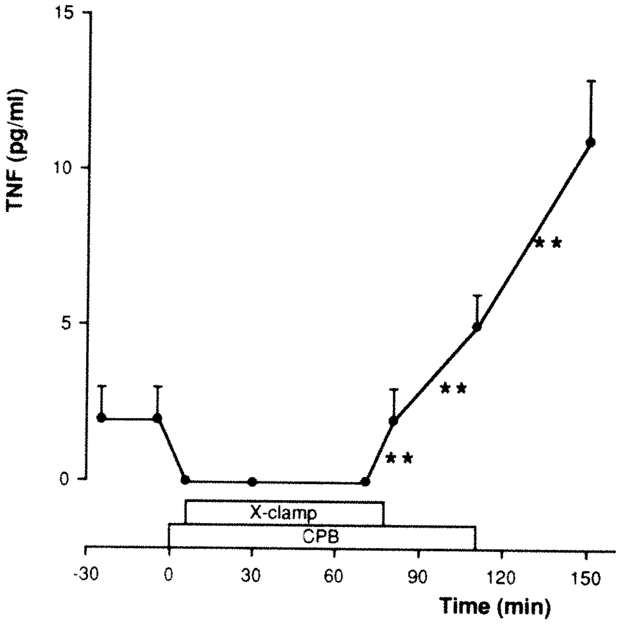


*Fig 3. Tumor necrosis factor (TNF) concentrations in plasma during and after cardiopulmonary bypass (CPB). There was a significant and steep increase in TNF concentration after release of the aortic cross-clamp (X-clamp). (**p < 0.01 versus 5 minutes before the clamp release.)*

Complement activation was shown by a steep increase in C3a after the start of CPB. This increase can be explained by complement activation either by the materials of the extracorporeal circuit [19] or by endotoxin released into the systemic circulation [20]. However, the contribution of both cannot be distinguished. The second increase in complement activation, after release of the cross-clamp, is in accordance with other studies and is thought to be due to the reperfusion of heart, lungs, and other poorly perfused tissues [21, 22]. It can be postulated that the release of endotoxin, at that same moment, is responsible for the increase in C3a, although no statistical evidence could be obtained for this hypothesis in the present study. Because endotoxin is known to activate the complement cascade through both the classic and the alternative pathway [20], it could also explain the observed activation of the classic pathway at the end of CPB in other studies [23].

The endotoxin release in the systemic circulation is thought to be responsible for the significant TNF formation seen at the end of CPB. In vivo studies showed that endotoxin induces TNF formation by activation of macrophages and monocytes with a peak concentration after 1 to 2 hours [24], which is in accordance with our results. We did not observe an increase in TNF after heparinization of the patient, whereas in vitro heparin seems to induce TNF production [25]. Also, all our samples were collected in EDTA, which prevents such artifacts.

Tumor necrosis factor is a mediator of general inflammation and induces fever, tachycardia, and hypotension [8, 26], which is also commonly observed in the postoperative course after CPB. In a recent study we demonstrated a significant increase in TNF during reperfusion after release of the aortic cross-clamp, which correlated with the hemodynamic instability after CPB [10]. These observations suggest that the release of endotoxin, induced by release of the cross-clamp, as discussed above, is responsible for the TNF formation in CPB and so can play an important role in the development of the postperfusion syndrome.

This study shows that the release of endotoxin, associated with the formation of TNF, plays an additional role in the development of the whole-body inflammatory reaction, independent of the material activation. As TNF is known to be a strong mediator in sepsis and endothelial injury, the release of endotoxin could play an important role in the generation of the adverse systemic effects of CPB. Therefore it seems important to focus on prevention and treatment of endotoxemia during CPB to improve the clinical course after CPB.

We thank the anesthetists and perfusionists of the Onze Lieve Vrouwe Gasthuis for their cooperation during the time of our study. Furthermore we thank J. Haan for his technical assistance in performing the assays. We especially thank Prof Dr H. S. A. Heijmans for critically reading the manuscript.

References

1. Westaby S. Organ dysfunction after cardiopulmonary bypass. A systemic inflammatory reaction by the extracorporeal circuit. Intensive Care Med 1987;13:89–95.
2. Kirklin JK, Westaby S, Blackstone EH, et al. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–57.
3. Chenoweth DE, Cooper SW, Hugli TE, et al. Complement activation during cardiopulmonary bypass. N Engl J Med 1981;304:497–503.
4. Hale DJ, Robinson JA, Loeb HS, Gunnar RM. Pathophysiology of endotoxin shock in man. In: Proctor RA, ed. Handbook of endotoxin. Vol 4. Amsterdam: Elsevier Science Publishing, 1986:1–17.
5. Morisson DC, Ryan JL. Endotoxins and disease mechanisms. Am Rev Med 1987;38:417–32.
6. Rocke DA, Gaffin SL, Wells MT, et al. Endotoxemia associated with cardiopulmonary bypass. J Thorac Cardiovasc Surg 1987;93:832–7.
7. Andersen LW, Baek L, Degn H, Lehd J, Krasnik M, Rasmussen JP. Presence of circulating endotoxins during cardiac operations. J Thorac Cardiovasc Surg 1987;93:115–9.
8. Beutler B, Cerami A. Cachectin: more than a tumor necrosis factor. N Engl J Med 1987;316:379–85.
9. Tracey KJ, Lowry SF, Fahey TJ III, et al. Cachectin/tumor necrosis factor induces fetal shock and stress hormone responses in the dog. Surg Gynecol Obstet 1987;164:415–22.
10. Jansen NJG, van Oeveren W, van der Broek, et al. Inhibition by dexamethasone of the reperfusion phenomena in cardiopulmonary bypass. J Thorac Cardiovasc Surg 1991;102:515–25.
11. Sturk A, Joop K, ten Cate JW, Thomas LM. Optimalization of a chromogenic assay for endotoxin in blood. In: ten Cate JW, Buller HR, Sturk A, Levin J, eds. Bacterial endotoxins: structure, biomedical significance, and detection with the limulus amebocyte lysate test. New York: Alan R. Liss, 1985:117–36.
12. Pearson FC, Wedry ME, Bohon J, Dabbah R. Relative potency of "environmental" endotoxin as measured by the limulus amoebocyte lysate test and the USP rabbit pyrogen test. New York: Alan R. Liss, 1982:65–77.
13. Fiddian-Green RG, Baker S. Predictive value of the stomach wall pH for complications after cardiac operations: comparison with other monitoring. Crit Care Med 1987;15:153–6.
14. Garthiram P, Gaffin SL, Wells MT, Brock-Utne JG. Superior mesenteric artery occlusion shock in cats: modification of the endotoxemia by antilipopolysaccharides antibodies. Circ Shock 1986;19:231–7.
15. Deitch EA, Berg R, Specian R. Endotoxin promotes the translocation of bacteria from the gut. Arch Surg 1987;122:185–90.
16. Deitch EA, Ma WJ, Ma L, Berg R, Specian RD. Endotoxin-induced bacterial translocation: a study of mechanisms. Surgery 1989;106:292–9.
17. Nolan JP. Endotoxin, reticuloendothelial function, and liver injury. Hepatology 1981;1:458–65.
18. Subramanian V, McLeod J, Gans H. Effect of extracorporeal circulation on reticuloendothelial function. I. Experimental evidence for impaired reticuloendothelial function following cardiopulmonary bypass in rats. Surgery 1968;64:775–84.
19. Kazatchkine MD, Nydegger UE. The human alternative pathway. Biology and immunopathology of activation and regulation. Prog Allergy 1982;30:193–234.
20. Vukajlovitch SW, Hoffman J, Morrison DC. Activation of human serum complement by bacterial lipopolysaccharides: structural requirements for antibody independent activation of the classical and alternative pathways. Mol Immunol 1987;24:319–32.
21. Engler RL, Schmid-Schonbein GW, Pavelec RS. Leukocyte capillary plugging in myocardial ischemia and reperfusion in the dog. Am J Pathol 1983;111:98–111.
22. Wildevuur ChRH, van Oeveren W. Blood interactions in extracorporeal circulation: tests to evaluate the activation of proteins and formed blood elements. Life Support Systems 1987;5:85–91.
23. Bonser RS, Dave JR, John L, et al. Complement activation before, during and after cardiopulmonary bypass. Eur J Cardiothorac Surg 1990;4:291–6.
24. Beutler B, Milsark IW, Cerami A. Cachectin/tumor necrosis factor: production, distribution, and metabolic fate in vivo. J Immunol 1985;135:3972–7.
25. Freeman R, Wheeler J, Robertson H, Paes ML, Laidler J. In-vitro production of TNF-a in blood samples. Lancet 1990;336:312–3.
26. Starnes HF Jr, Warren RS, Jeevanandam M, et al. Tumor necrosis factor and the acute metabolic response to tissue injury in man. J Clin Invest 1988;82:1321–5.

INVITED COMMENTARY

The current support system of cardiopulmonary bypass (CPB) is known to induce a generalized inflammatory response, which in its severe form may induce multiorgan dysfunction as the "postperfusion syndrome."

Based on the observations from this and a previous paper [10], Dr Jansen and colleagues proposed that the appearance of endotoxin in the circulation of patients on CPB results in the release of tumor necrosis factor (TNF), which then plays an important role in the mechanism of the inflammatory-type responses during and after exposure to CPB.

A number of recently published studies have indicated that cytokines may be a significant component of the physiologic response to CPB. This article proposes that one of the initiating events of cytokine production is exposure to endotoxins that appear before and after CPB. This hypothesis is consistent with data generated in several experimental systems that have shown that exposure of monocytes and macrophages to endotoxin results in the production of various cytokines including interleukin-1, interleukin-8, and TNF. Dr Jansen and colleagues discuss several possible mechanisms for the sources and kinetics of endotoxin release during CPB.

It should be noted that these mechanisms, including the proposal that endotoxin results in TNF release, are speculative until a direct causal relationship is established. At this time, we only know that there is an association between the appearance of endotoxin, C3a, and TNF. The hypothesis that Dr Jansen and colleagues present and their speculations on the mechanisms of endotoxin release are readily testable with the appropriate reagents. One possible experiment is the systematic administration of endotoxins in an animal model of CPB. If their hypothesis is correct, then it would be expected that an increase in TNF release would correlate with the amount of endotoxin administered. Furthermore, the model would predict that increasing levels of endotoxin would result in adverse systemic effects of the type seen in postperfusion syndrome. The role of TNF in the chain of events could be directly tested by the administration of monoclonal antibodies to TNF before, during, and after the exposure to endotoxin. If the role of TNF is as important as Dr Jansen and colleagues suggest, then blocking the effects of TNF with antibody should significantly change the pathology that can follow CPB.

We believe that the importance of establishing direct relationships cannot be overemphasized because they provide insights into the mechanisms of postperfusion syndrome that cannot be attained by other means. Thus, although the hypothesis proposed here is interesting, the details of the mechanisms need to be tested to determine its validity.

James F. George, PhD
James K. Kirklin, MD

Division of Cardiothoracic Surgery
Department of Surgery
Rm 739 ZRB
UAB Station
University of Alabama at Birmingham
Birmingham, AL 45239

Temperature Monitoring During CPB in Infants: Does It Predict Efficient Brain Cooling?

Frank H. Kern, MD, Richard A. Jonas, MD, John E. Mayer, Jr, MD,
Frank L. Hanley, MD, Aldo R. Castaneda, MD, and Paul R. Hickey, MD

Departments of Anesthesiology and Cardiac Surgery, The Children's Hospital, Boston, and Harvard Medical School, Boston, Massachusetts

We examined jugular venous oxygen saturation data in 17 pediatric patients less than 1 year of age undergoing hypothermic cardiopulmonary bypass (CPB). Jugular venous oxygen saturations (JvO_{2SAT}s) were measured before bypass and during the active core cooling portion of CPB. The study intervals during CPB included 1 minute after initiation of CPB, at a tympanic membrane temperature of 15°C, and at a rectal temperature of 15°C. During these measurement intervals, there were no significant changes in mean arterial pressure, pump flow rate, arterial oxygen saturation, mixed venous oxygen saturation, carbon dioxide tension, or hematocrit. Six of the 17 patients (29%) demonstrated a significantly lower JvO_{2SAT} (87.1% ± 6.3% versus 98.1% ± 0.9%) at a tympanic membrane temperature of 15°C. Patients demonstrating jugular venous desaturation could not be predicted from continuous monitoring of tympanic membrane and rectal temperatures or through on-line measurements of mixed venous oxygen saturation. Low JvO_{2SAT} suggests higher levels of cerebral metabolism and cerebral uptake of oxygen. In the presence of deep hypothermic CPB and stable anesthetic levels, the most likely cause of a low JvO_{2SAT} is inadequate cerebral cooling. We believe JvO_{2SAT} monitoring may be an important adjunct to conventional temperature monitoring in the patient undergoing deep hypothermic CPB or total circulatory arrest.

(Ann Thorac Surg 1992;54:749–54)

The use of deep hypothermic cardiopulmonary bypass (CPB) with or without total circulatory arrest (TCA) has substantially improved operating conditions in neonates and infants, resulting in improved survival and reduced cardiac morbidity [1]. However, as overall surgical outcome improves, neuropsychiatric dysfunction has become a more prominent and visible complication in congenital heart patients [2–5].

Recent reports suggest that transient and permanent neuropsychiatric injury occurs in as much as 25% of all infants undergoing hypothermic cardiopulmonary bypass with or without circulatory arrest [2]. In complex palliative repairs, such as hypoplastic left heart syndrome, neurologic injury has been reported to be as high as 45% [3]. These uncomfortably high percentages of neuropsychiatric impairment are disturbing and suggest fundamental problems in our ability to provide effective cerebral protection during CPB.

Currently, the most effective means of protecting the brain from CPB- or TCA-induced injury is hypothermia [6–10]. Hypothermia reduces the metabolic rate of the brain and preserves cellular stores of high-energy phosphates [8, 9]. With effective cooling, the brain's metabolic rate falls exponentially with temperature [7]. Effective cerebral cooling therefore is critical to brain protection. If the brain does not cool evenly or thoroughly, then selective regions of the brain may be at higher risk for cerebral injury. Ineffective cerebral cooling should be reflected in increased oxygen extraction across the brain and low jugular venous oxygen saturation (JvO_{2SAT}). Recent evidence suggests that brain cooling may not in fact be homogeneous and that conventional estimates of brain temperature using tympanic membrane or nasal pharyngeal probes may not accurately reflect residual temperature gradients within the brain [7, 11–15]. Therefore, a major cause of cerebral injury during CPB and TCA maybe unexpectedly high cerebral metabolism due to incomplete cerebral cooling. We hypothesized that JvO_{2SAT} monitoring may identify patients at risk for cerebral injury due to higher than anticipated cerebral metabolism. We tested this hypothesis in 17 infants undergoing deep hypothermic CPB with or without TCA for repair of congenital heart defects.

Material and Methods

Patients

After the committee of clinical investigation's approval and informed parental consent, 17 pediatric patients undergoing deep hypothermic CPB for repair of complex congenital heart defects were studied. Patients were all less than 1 year of age with a range of 2 to 210 days. Twelve of the 17 patients were less than 1 month of age. Patients with preexisting neurologic dysfunction were excluded from the study. The study was conducted over a period of 13 months, commencing in September 1990 and concluding in September 1991.

Accepted for publication Feb 21, 1992.

Address reprint requests to Dr Kern, Duke University Medical Center, Box 3046, Durham, NC 27710.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Anesthetic Management

No premedication was administered to the study patients. Anesthetic management was uniform in all patients and consisted of fentanyl, 100 to 150 μg/kg, midazolam, 0.0 to 0.2 mg/kg, incremental doses of pancuronium for neuromuscular blockade, and controlled mechanical ventilation. No additional inhalation anesthetic drugs or cerebral vasoactive agents were administered.

Cardiopulmonary Bypass Management

During CPB, the extracorporeal circulation was maintained using nonpulsatile pump flow and a membrane oxygenator. The pump-oxygenator system was primed with Normosol-R (250 to 650 mL), heparin (15,000 to 17,000 U), whole blood (200 to 500 mL to achieve a hematocrit of 0.20 ± 0.02 during CPB), mannitol (0.5 to 1 g/kg), sodium bicarbonate (to achieve a pH of 7.35 to 7.45), and methylprednisolone (30 mg/kg).

All patients were cooled to deep hypothermic temperatures of 13° to 15°C using a combination of surface and core cooling. Surface cooling began in the prebypass period and continued throughout the hypothermic period of CPB. A cooling blanket set at 4°C, a room temperature of 18.3°C and ice bags placed on either side of the patient's head constituted the method of surface cooling. Core cooling began with the initiation of CPB by maintaining the water temperature of the heat exchanger at 4° to 5°C until the rectal temperature (T_R) and tympanic membrane temperature (T_{TM}) were 15°C or less. Blood gas management during CPB was directed at maintaining a pH of 7.35 to 7.40 and a carbon dioxide tension of 35 to 40 mm Hg, uncorrected for body temperature using the principles of alpha-stat blood gas management. One hundred percent oxygen was administered through the fresh gas inlet of the oxygenator. Arterial oxygen tension was monitored throughout CPB and maintained between 400 and 700 mm Hg.

Study Protocol

Three temperature probes (tympanic membrane, nasal pharyngeal, and rectal) were placed in all 17 patients and monitored continuously throughout the study period. In the prebypass period, comparisons of T_{TM} and nasal pharyngeal temperature (T_{NP}) were made to assure appropriate probe placement. Differences of 0.2°C or more between T_{TM} and T_{NP} suggested an abnormal probe placement, and either probe was repositioned. Once the chest and pericardium were opened, a 3F catheter was surgically placed into the superior vena cava and advanced to the jugular venous bulb. The tail end of the catheter was passed over the ether screen to allow intermittent sampling of jugular venous blood.

At four predefined intervals, blood samples were drawn simultaneously from an indwelling arterial catheter (radial, umbilical, or femoral) and the jugular venous catheter. The sampling intervals were (1) before initiation of CPB, (2) 1 minute after initiation of CPB, (3) at a T_{TM} of 15°C, and (4) at a T_R of 15°C. In patients in whom the T_R cooled more rapidly then the T_{TM} a fifth blood sample was obtained 3 to 4 minutes after the T_{TM} and T_R were both 15°C or less. At each interval, blood samples were drawn and analyzed by cooximetry for determination of arterial oxygen saturation (SaO_2) and JvO_{2SAT}. Additionally, measurements of carbon dioxide tension, oxygen tension, and hematocrit were maintained over a narrow range to minimize metabolic influences on the cerebral vasculature and the distribution of blood flow to the brain. At each study interval mean arterial pressure, T_{TM}, T_{NP}, and T_R were recorded. Once cardiopulmonary bypass was initiated, mixed venous oxygen saturation (MvO_2) was continuously monitored from the venous limb of the extracorporeal circuit.

Data Analysis

All data were reported as mean ± standard deviation for all measured parameters. Based on differences in JvO_{2SAT} obtained at a T_{TM} of 15°C, patients were separated into two groups (A and B). Temperature, oxygen saturation, and demographic data were compared for differences between groups A and B using the Wilcoxon rank-sum test. Intragroup differences in temperature, MvO_2, SaO_2, pump flow rate, mean arterial pressure, age, and patient's weight were compared using the unpaired Student's *t* test and 2×2 contingency tables using Fisher's exact test. The relationships between MvO_2 and JvO_{2SAT} and between SaO_2 and JvO_{2SAT} were compared using simple linear regression analysis. Two methods were used to evaluate the relationship between JvO_{2SAT} and cooling time: (1) data from groups A and B were pooled and analyzed by regression analysis. Each group's regression data were compared at the 95% confidence interval for a JvO_{2SAT} of +98%. (2) A multiple curve modeling technique was used to determine the best fit of the data. With the second method estimates of the length of cooling time required for the JvO_{2SAT} to reach full (98% to 100%) saturation were obtained by graphing JvO_{2SAT} versus cooling time for each individual patient. These points were then extrapolated to a fully saturated JvO_{2SAT}. Groups A and B were then compared using the Wilcoxon rank-sum test. Statistical significance was accepted at *p* values ≤ 0.05.

Results

Table 1 contains demographic data for the 17 patients studied, including diagnosis and operative procedure performed. Based on JvO_{2SAT} data obtained at a T_{TM} of 15°C, two distinct groups were identified (Table 2). In group A (11/17 patients or 71%), JvO_{2SAT}s were fully saturated. Group A patients had JvO_{2SAT} values of 98.1% ± 0.9% with an SaO_2 to JvO_{2SAT} difference of 0.3% ± 0.4%. In group B (6/17 patients or 29%), the JvO_{2SAT} data were significantly lower. Group B patients had JvO_{2SAT} values of 87.1% ± 6.3%, with an SaO_2 to JvO_{2SAT} difference of 11.4% ± 6.9%. Despite the considerable differences in JvO_{2SAT} and SaO_2 to JvO_{2SAT} differences, traditionally monitored variables such as cooling time, T_{TM}, T_{NP}, and T_R were not statistically different between the two groups (see Table 2). The MvO_2 and SaO_2 values correlated poorly with the JvO_{2SAT} data (*r* values of 0.22

Table 1. Demographic Data

Diagnosis	Operation	Age (days)	Weight (kg)	Jugular Venous Desaturation	Cooling Pattern (T_{TM}-T_R)
TGA/IVS	Arterial switch	6	3.6	Yes	Reversed
TGA/IVS	Arterial switch	3	3.0	Yes	Customary pattern
TGA/IVS	Arterial switch	13	3.5	No	Same rate
TGA/PS/ASD/VSD	Rastelli	70	3.7	Yes	Customary pattern
TGA/IVS/PDA	Arterial switch	30	4.6	Yes	Customary pattern
TGA/IVS	Arterial switch	2	3.5	No	Same rate
TOF	TOF repair	210	7.9	No	Same rate
Truncus type I	Truncus repair	11	2.7	No	Same rate
TGA/IVS	Arterial switch	2	4.1	No	Customary pattern
TGA/IVS	Arterial switch	4	3.7	No	Customary pattern
TGA/IVS	Arterial switch	3	3.6	No	Reversed
CAVC	CAVC repair	66	4.9	No	Same rate
TOF	TOF repair	205	7.1	No	Same rate
TGA/IVS	Arterial switch	4	3.7	No	Customary pattern
TGA/VSD	Arterial switch	31	4.3	No	Reversed
HLHS	Stage I palliation	7	3.0	Yes	Same rate
TGA/IVS	Arterial switch	4	3.4	Yes	Reversed

ASD = atrial septal defect; CAVC = complete atrioventricular canal; HLHS = hypoplastic left heart syndrome; IVS = intact ventricular septum; PDA = patent ductus arteriosus; PS = pulmonary valve stenosis; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; T_R = rectal temperature; T_{TM} = tympanic membrane temperature; VSD = ventricular septal defect.

and 0.52, respectively). The MvO_2 data are graphically demonstrated in Figure 1.

Jugular venous desaturation occurred more commonly in neonates than in older infants (not significant). Of the 6 patients demonstrating JvO_{2SAT} desaturation, 5 were less than 1 month of age (neonates). The sixth patient was 70 days of age. Overall, 5 of 12 neonates (42%) demonstrated jugular venous desaturation, whereas only 1 of the 5 remaining infants (20%) had low jugular venous saturations measured at a T_{TM} of 15°C.

Table 2. Jugular Venous Saturation Data Obtained at a Tympanic Membrane Temperature of 15°C

Parameter	High JvO_{2SAT} (n = 11)	Low JvO_{2SAT} (n = 6)
JvO_{2SAT} (%)	98.1 ± 0.8[a]	87.1 ± 5.75[a]
SaO_2 (%)	98.4 ± 0.6	98.3 ± 0.7
$SaO_2 - JvO_{2SAT}$ (%)	0.3 ± 0.41[a]	11.4 ± 6.9[a]
MvO_2 (%)	95.7 ± 1.5	94.0 ± 1.4
Cooling time (min)	8.4 ± 2.0	7.5 ± 0.8
T_R (°C)	15.8 ± 3.3	16.8 ± 3.4
T_{NP} (°C)	14.1 ± 1.4	15.1 ± 2.3
T_{TM} (°C)	14.9 ± 0.29	14.8 ± 0.5
Age (days)	34.5 ± 64	22.6 ± 29
Weight (kg)	6.4 ± 3.4	4.1 ± 0.7
$PaCO_2$ (mm Hg)	37 ± 3.3	36 ± 3.0
Pump flow rate (mL/kg)	144 ± 12	129 ± 25
MAP (mm Hg)	32 ± 8.7	34 ± 9

[a] $p < 0.05$.

JvO_{2SAT} = jugular venous oxygen saturation; MAP = mean arterial pressure; MvO_2 = mixed venous oxygen saturation; $PaCO_2$ = carbon dioxide tension; SaO_2 = arterial oxygen saturation; T_{NP} = nasal pharyngeal temperature; T_R = rectal temperature; T_{TM} = tympanic membrane temperature.

The diagnoses of the 6 patients demonstrating jugular venous desaturation include transposition of the great arteries (TGA) with intact septum in 4, complex TGA (consisting of an atrial septal defect, a ventricular septal defect, and pulmonary valve stenosis) in 1, and hypoplastic left heart syndrome in 1. The patient with complex TGA was 70 days of age (see Table 1). It is interesting to note that all 6 of these patients required a modified aortic cannulation site. The aortic cannula was placed in a distal

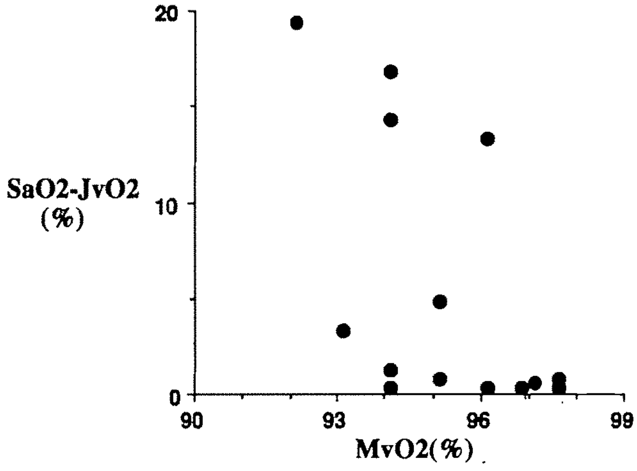


Fig 1. Arterial venous oxygen saturation difference across the brain (SaO2-JvO2) and mixed venous oxygen saturation (MvO2). There is a very poor correlation between mixed venous oxygen saturation and high oxygen saturation differences across the brain.

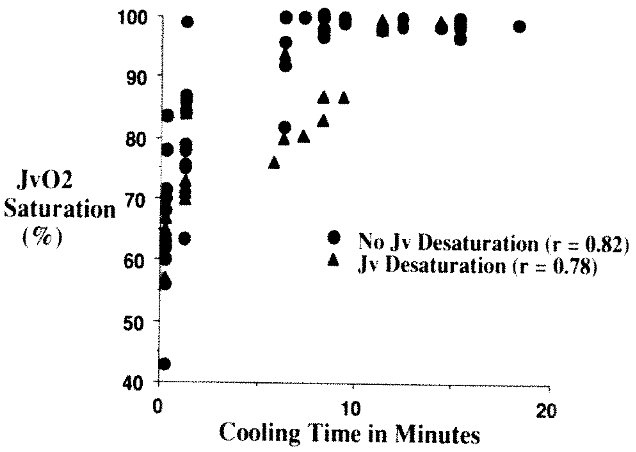


Fig 2. Jugular venous oxygen (JvO2) saturation is plotted against cooling time. The solid circles *represents group A patients (no jugular venous [Jv] desaturation at 15°C), and the* solid triangles *represent group B patients (Jv desaturation at a T_{TM} of 15°C). Cooling rates for both groups is best depicted by a logarithmic relationship. This graph suggests that Jv saturations take longer to reach full saturation in the group B patients.*

position in the ascending aorta in all 5 patients with transposition and was placed in the main pulmonary artery in the patient with hypoplastic left heart syndrome. None of the 4 patients with a conventional cannulation site demonstrated jugular venous desaturation at a T_{TM} of 15°C.

Figure 2 demonstrates the logarithmic relationship between jugular venous saturation and cooling time. Patients who were desaturated when a T_{TM} of 15°C was first reached subsequently had development of full saturation after a longer cooling interval. By regression analysis (95% confidence limits), group A patients achieved full JvO_{2SAT} 8.43 minutes after the initiation of CPB, whereas the group B patients achieved full JvO_{2SAT} 11.75 minutes after the initiation of CPB. A second method used to approximate the length of time required to achieve full jugular venous saturation (+98%) employed a multiple curve modeling technique. In this approach, the individual JvO_{2SAT} values obtained during the cooling phase of CPB were extrapolated toward the point of full jugular venous saturation. The time required to reach complete jugular venous saturation in group A patients was 8.1 ± 1.4 minutes (range, 6.0 to 10.1 minutes), whereas in group B patients, full jugular venous saturations were not achieved until a cooling period of 10.7 ± 1.2 minutes (range, 9.3 to 12.3 minutes). These data were statistically different at a *p* value of 0.01 using the Wilcoxon sign rank test (Fig 3).

In older children and adults, the head (represented by the T_{TM}) cools more rapidly than the rectal temperature. In this study, however, three distinct cooling patterns were observed: a reverse cooling pattern in which the rectal temperature cooled more rapidly than the T_{TM}, a more customary cooling pattern in which the T_{TM} cooled much more rapidly than the T_R, and a cooling pattern in which the T_{TM} and T_R cooled either at the same rate or the T_{TM} cooled only slightly more rapidly than the T_R. Jugular venous desaturations were observed with all three cooling patterns (see Table 1).

The reversed cooling pattern was observed in 4 patients. Two of these patients demonstrated jugular venous bulb desaturation at a T_{TM} of 15°C. Because T_R decreased more rapidly than T_{TM}, and T_{TM} and T_{NP} were virtually identical (*r* value, 0.87), jugular venous desaturation was present in 2 patients after all three measured temperatures were at or below 15°C. Because of the potential impact this finding may have on conventional temperature monitoring, an additional set of blood samples was obtained 3 to 4 minutes after the T_{TM} and T_R were both 15°C or less. Measured JvO_{2SAT}s obtained after this extended cooling period were +98%, ie, jugular venous desaturations were no longer present.

In the 17 patients studied, the mean cooling times required for all three temperatures (T_{TM}, T_{NP}, and T_R) to be 15°C or less and to eliminate jugular venous desaturation were 12.70 ± 3.5 minutes for group A and 12.35 ± 1.8 minutes for group B (Table 3). Although overall cooling times were similar between the two groups, group B

Fig 3. Individual jugular venous oxygen (JvO2) saturation data are plotted versus cooling time for cardiopulmonary bypass samples for all 17 patients. For each individual patient, the bypass measurements of JvO2 saturation are extrapolated to a point of 100% jugular venous saturation. Group A patients are represented by squares *(both solid and open), and group B patients are represented by* circles *(both solid and open).* Open squares *and* circles *designate patients who had a reverse cooling pattern. Mean times required to reach the extrapolation point were 8.1 ± 1.4 minutes for group A and 10.7 ± 1.2 minutes for group B. These differences were statistically significant* (p ≤ *0.01).*

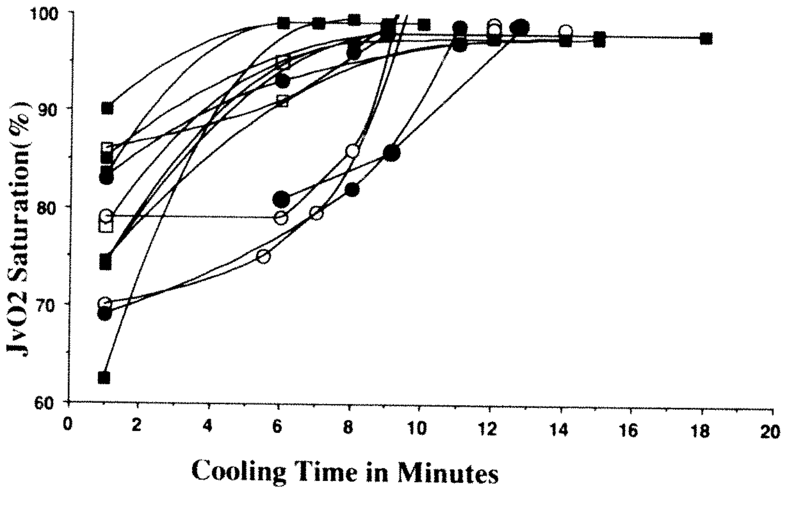


Table 3. Jugular Venous Saturation Data Obtained at Tympanic Membrane and Rectal Temperatures of 15°C[a]

Parameter	High JvO_{2SAT} (n = 11)	Low JvO_{2SAT} (n = 6)
JvO_{2SAT} (%)	97.9 ± 1.1	97.8 ± 0.9
SaO_2 (%)	98.3 ± 1.0	98.5 ± 0.8
$SaO_2 - JvO_{2SAT}$(%)	0.33 ± 0.47	0.67 ± 0.64
MvO_2 (%)	95.0 ± 1.4	95.0 ± 1.7
Cooling time (min)	12.7 ± 3.5	12.3 ± 1.8
T_R (°C)	15.0 ± 1.2	14.9 ± 2.9
T_{NP} (°C)	13.2 ± 1.4	15.4 ± 2.8
T_{TM} (°C)	13.9 ± 1.4	14.6 ± 2.9
$PaCO_2$ (mm Hg)	35 ± 4.1	34 ± 3.3
Pump flow rate (mL/kg)	117 ± 30	121 ± 25
MAP (mm Hg)	32 ± 9	27 ± 9

[a] Includes 2 patients with a reverse cooling pattern whose sample was obtained 3 to 4 minutes after tympanic membrane temperature reached 15°C.

Abbreviations are as in Table 2.

patients required a significantly longer period of cooling to eliminate jugular venous desaturation (8.1 ± 1.4 minutes for group A versus 10.7 ± 1.2 minutes for group B). In the 2 patients with reverse cooling, jugular venous desaturation persisted despite a T_{TM}, T_{NP}, and T_R of 15°C or less.

Formalized neuropsychiatric testing was not employed in this study. However, the study patients were evaluated for evidence of gross neurologic deficits throughout their intensive care unit stay. None of the 17 patients studied demonstrated postoperative seizures, movement disorders, or focal neurologic deficits at the time of discharge from the pediatric cardiac intensive care unit.

Comment

Several studies have evaluated cerebral metabolism during deep hypothermic CPB in children and have shown a marked reduction in cerebral metabolism at deep hypothermic temperatures [7–9]. These studies strongly support cerebral hypothermia as the most important component of brain protection during CPB. Few data, however, are currently available about the efficiency of CPB in cooling the brain. Studies of cerebral ischemic injury suggest that brain cooling is not uniform and that temperature monitoring of superficial brain tissue correlates poorly with temperature monitoring of deeper brain structures [11–15].

Clinical data have suggested nonhomogenous cerebral cooling as a source of brain injury. Bellinger and associates [16] suggested that the length of time allowed for cerebral cooling before the institution of circulatory arrest correlates with the presence of neuropsychiatric dysfunction. More recently, Greeley and colleagues [7] demonstrated that cerebral metabolic rates vary widely despite cooling times of 20 minutes and rectal and nasal pharyngeal temperatures of 18°C. Greeley and colleagues' work specifically describes 3 patients with abnormally high cerebral metabolic rates obtained just before the initiation of TCA. All three of these patients demonstrated postoperative neurologic dysfunction (2 with seizures, 1 with choreoathetosis).

Based on these observations, we attempted to better characterize brain cooling with the use of JvO_{2SAT} monitoring during CPB. We believe that low JvO_{2SAT}s reflect higher levels of both cerebral metabolism and oxygen uptake by the brain. In the context of hypothermic CPB, low JvO_{2SAT} most likely indicates incomplete cerebral cooling, due to inadequate delivery of cold perfusate to the brain.

Our data demonstrate that jugular venous oxygen desaturation was present in 29% of infants when their T_{TM} reached 15°C. The presence of low JvO_{2SAT} reflects a reduced efficiency in cerebral cooling that cannot be appreciated by conventional temperature or mixed venous oxygen saturation monitoring alone. We believe that patients demonstrating jugular venous desaturation may be at an increased risk of neurologic injury, especially if TCA is instituted after a relatively brief period of cooling. Cooling times required to reach full jugular venous saturation in the low JvO_{2SAT} group ranged from 10 to 12.3 minutes based on extrapolating each patient's jugular venous saturation to 98% to 100%. The time required to ensure maximal jugular venous saturation, however, remains unknown and may vary based on biologic variability within the patient population, characteristics of aortic cannula flow, or institutional differences in CPB management.

Suggesting causes for the variability in cooling time required for JvO_{2SAT} variability is difficult. Saturation differences may simply reflect biologic differences between patients. However, it is interesting to note that jugular venous desaturation was more likely to occur in neonates and particularly in patients with modified aortic cannula placement. Neonates have a smaller ascending aorta. When the conventional aortic cannulation site is moved, as occurs in TGA and hypoplastic left heart syndrome, the distribution of cold perfusate may be preferentially directed away from the brain.

In the arterial switch procedure for TGA, the coronary arteries are translocated to the aortic root. To facilitate coronary transfer, the aortic cannula is placed as far from the aortic root as possible. In this position, the tip of the aortic cannula may promote preferential flow down the aorta or induce a Venturi effect to steal flow from the cerebral circulation. This would also help explain the reverse cooling pattern observed in 4 of our patients with TGA.

In the stage I repair of hypoplastic left heart syndrome, the aorta cannot be cannulated due to the extreme hypoplasia of the ascending aorta. Instead, the arterial cannula is placed in the main pulmonary artery. The head vessels are perfused in a retrograde fashion through the ductus. This type of arterial perfusion may result in reduced efficiency in the distribution of cold perfusate to the cerebral circulation.

Institutional variability in CPB management may be an additional factor. In this study, the water bath of the heat exchanger was set at 4°C and the patient was rapidly cooled until all monitored temperatures were 15°C or less. In other institutions cooling is more gradual. Water bath temperature is slowly lowered to maintain an arterial inflow to water bath temperature gradient of 10°C or less. Under these conditions cerebral cooling may be slower.

Two potential methodologic flaws in this study include jugular venous catheter and T_{TM} probe placement. Although jugular venous catheter placement was not confirmed radiographically, jugular venous bulb samples were compared with on-line measurements of MvO_2. In patients demonstrating jugular venous desaturation, MvO_2 measurements were uniformly higher (see Fig 1). Blood samples demonstrating jugular venous desaturation were therefore not due to admixture of systemic venous blood.

Tympanic membrane temperature measurements are used routinely at our institution. A strong correlation between T_{TM} and T_{NP} measurements strongly supports that malplacement of the tympanic probe was not a factor.

In conclusion, we demonstrated that cerebral cooling efficiency based on monitored jugular venous saturation is quite variable and is not uniformly predicted by conventional temperature monitoring alone. Factors such as biologic variability of the patient, aortic cannulation site, and perfusion technique may play a role in cerebral perfusion during hypothermic CPB. Our findings suggest that jugular venous monitoring may be an important adjunctive monitor for children undergoing low-flow CPB or TCA.

References

1. Castaneda AR, Mayer JE Jr, Jonas RA, Lock JE, Wessel DL, Hickey PR. The neonate with critical congenital heart disease: repair—A surgical challenge. J Thorac Cardiovasc Surg 1989;98:869–75.
2. Ferry PC. Neurologic sequelae of open-heart surgery in children. Am J Dis Child 1990;144:369–73.
3. Glauser TA, Rorke LB, Weinberg PM, Clancy RR. Acquired neuropathologic lesions associated with the hypoplastic left heart syndrome. Pediatrics 1990;85:991–1000.
4. Blackwood MJ, Haka-Ikse K, Steward DJ. Developmental outcome in children undergoing surgery with profound hypothermia. Anesthesiology 1986;65:437–40.
5. DeLeon S, Ilbawi M, Arcilla R, et al. Choreoathetosis after deep hypothermia without circulatory arrest. Ann Thorac Surg 1990;50:714–9.
6. Michenfelder JD. The hypothermic brain. In: Michenfelder JD, ed. Anesthesia and the brain. New York: Churchill Livingstone, 1988:23–34.
7. Greeley WJ, Kern FH, Ungerleider RM, et al. The effect of hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral metabolism in neonates, infants and children. J Thorac Cardiovasc Surg 1991;101:783–94.
8. Swain JA, McDonald TJ, Griffith PK, Balabal RS, Clark RE, Ceckler T. Low flow hypothermic cardiopulmonary bypass protects the brain. J Thorac Cardiovasc Surg 1991;102:76–84.
9. Norwood WI, Norwood CR, Ingwall JS, Castenada AR, Fossel ET. Hypothermic circulatory arrest: 31-phosphorus nuclear magnetic resonance of isolated perfused neonatal rat brain. J Thorac Cardiovasc Surg 1979;78:823–30.
10. Norwood WI, Norwood CR, Castaneda AR. Cerebral anoxia: effect of deep hypothermia and pH. Surgery 1979;86:203–10.
11. Mellergard P, Nordstrom C. Epidural temperature and possible intracerebral temperature gradients in man. Br J Neurosurg 1990;4:31–8.
12. Serota HM, Gerard RW. Localized temperature changes in the cat brain. J Neurophysiol 1983;1:115–24.
13. Busto R, Dietrich WD, Globus MY, Valdes I, Scheinberg P, Ginsberg MD. Small differences in the intra-ischemic brain temperature critically determine the extent of ischemic neuronal injury. J Cereb Blood Flow Metab 1987;7:729.
14. Busto R, Mordecai Y-T, Dietrich D, Martinez E, Valdes I, Ginsberg MD. Effects of mild hypothermia on brain ischemia. Stroke 1989;20:904–10.
15. Okada Y, Tanimoto M, Yoneda K. The protective effect of hypothermia on reversibility in the neuronal function of the hippocampal slice during long lasting anoxia. Neurosci Lett 1988;84:277–82.
16. Bellinger PC, Wernovsky G, Rappaport LA, et al. Cognitive development of children following early repair of transposition of the great arteries using deep hypothermic circulatory arrest. Pediatrics 1991;87:701–8.

Surgical Management of Infective Endocarditis in Children

Michael Citak, MD, Allan Rees, MD, and Constantine Mavroudis, MD

Departments of Surgery and Pediatrics, University of Louisville, Louisville, Kentucky

Infective endocarditis occurs infrequently in the general pediatric population, occurring mostly in patients with congenital heart disease. This study reviews our surgical experience with infective endocarditis based on a policy of aggressive intervention, conservative operative debridement, and creative reconstruction options using pericardium and prosthetic heart valves. From 1982 to 1989, 16 patients, 3 weeks to 16 years of age, underwent 19 intracardiac operations for infective endocarditis therapy at Kosair Children's Hospital. Eight (42%) were for resection of vegetations alone; an additional 11 operations (58%) involved more extensive debridements requiring either valve replacement or valvuloplasty using pericardium for exclusion of an abscess cavity, closure of a fistula, or for valve repair. Operative mortality was 25% (4 patients) and related to preoperative disease severity. There was one late death. Offending organisms included *Staphylococcus* species (31%), *Haemophilus influenzae* (13%), pneumococcus (5%), gram-negative organisms (13%), and *Candida* (13%); no organism grew on culture in 25%. We conclude that aggressive surgical exploration in patients with infective endocarditis is indicated and often requires resection of vegetations alone. More extensive procedures should preserve as much valvular tissue as possible. Pericardium is useful for reconstruction after debridement.

(Ann Thorac Surg 1992;54:755–60)

Infective endocarditis occurs relatively infrequently in children under 17 years of age [1–3]. At highest risk are those patients with congenital heart disease [1–8]. To a lesser degree, endocarditis complicates patients with rheumatic heart disease, and rarely those with no major heart disease [1, 4–7, 9]. Reports by Johnson and Rhodes [1] and Karl and associates [4] have shown that the most frequent congenital malformations that predispose to the development of endocarditis are tetralogy of Fallot, ventricular septal defect, and patent ductus arteriosus [5, 7, 10]. Endocarditis complicating open heart operations is associated with a higher mortality rate than those cases occurring in patients who have not had a recent cardiac operation [4].

The organisms most commonly isolated are *Staphylococcus aureus*, *Streptococcus viridans*, and *Streptococcus hemolyticus* [1, 4, 5, 7]. Less frequently infecting organisms are *Haemophilus influenzae*, various gram-negative organisms, and *Candida albicans* [1, 3–5, 7, 10]. Bloodstream entry of the infecting organism is infrequently identified. Bone, pulmonary, and cutaneous infections, as well as dental manipulations, have all been described as possible sources for bacteremia [1, 4–7, 10, 11]. However, in more than 50% of patients with documented bacteremias, no source of contamination has been identified.

Patient survival is dependent on several factors, which include early diagnosis, initiation of appropriate antimicrobial therapy, and preservation or restoration of cardiac function. The purpose of this retrospective analysis is to report our surgical experience with infective endocarditis in children and emphasize guidelines for conservative and restorative therapy.

Material and Methods

From 1982 to 1989, 21 patients were treated for infective endocarditis at Kosair Children's Hospital, Louisville, Kentucky. In 5 patients (4 of whom had preexisting congenital heart disease) medical management, consisting of specific long-term antibiotic therapy, resulted in resolution without further complications. Table 1 summarizes the clinical characteristics and outcome of these patients. The remaining 16 patients (76%) underwent one or more cardiac operations as part of their treatment for infective endocarditis and are the subjects of this report. The age at operation ranged from 3 weeks to 16 years, with 7 patients being less than 2 years old. Patients received a multidisciplinary approach to their care, involving thoracic surgery, pediatric medicine, cardiology, and infectious disease consultation. Endocarditis was diagnosed on the basis of clinical and laboratory criteria that included cardiac murmur development or change in a septic patient, fever with no other identifiable source, signs of systemic septic embolization, and positive blood cultures. All patients had abnormal echocardiograms revealing hemodynamically significant valvular abnormalities, the presence of vegetations, or both (Fig 1). Indications for operation included unresolving sepsis in patients with vegetations on echocardiography or persistent heart failure stemming from damaged valves. All but 1 patient had exploration in the acute phase of infection. Operations were performed

---

Accepted for publication Feb 24, 1992.

Address reprint requests to Dr Mavroudis, Division of Cardiovascular-Thoracic Surgery, The Children's Memorial Hospital, M/C #22, 2300 Children's Plaza, Chicago, IL 60614.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Clinical Characteristics of Medical Therapy Patients

Patient	Sex	Age (y)	Clinical Presentation	Preexisting Defect	Blood Culture Isolates	Treatment and Outcome
A	F	2	Fever, anorexia, anemia; tricuspid vegetation (septal leaflet) on ECHO	Small VSD	*Haemophilus influenzae* type B	6 wk IV ceftriaxone; vegetation resolved by ECHO; VSD closed 1 year later
B	F	1.3	Fever, anorexia, anemia; leukocytosis, iESR; vegetation on right side of atrial septum by ECHO	No congenital heart defect	Coagulase-positive *Staphylococcus aureus*	6 wk IV oxacillin; vegetation resolved by ECHO; patient recovered
C	M	7	Fever, anorexia, anemia; leukocytosis, iESR; no vegetations by ECHO	Remote postop for IAA (tube graft) and VSD (closure)	*Haemophilus influenzae* type B	6 wk IV ceftriaxone; ECHO remained normal; patient recovered
D	M	10	Fever, anorexia, leukocytosis, iESR; mitral and pulmonary valvular vegetations by ECHO	Double-inlet single left ventricle with d-transposition; PS	α-Hemolytic *Streptococcus*	6 wk IV penicillin; vegetations resolved on ECHO; successful modified Fontan 1 y later
E	M	0.3	Fever, leukocytosis, iESR; no vegetations by ECHO	Tricuspid atresia with PS; postop systemic-to-PA shunt	Coagulase-negative *Staphylococcus aureus*	6 wk IV vancomycin; ECHO remained normal; awaiting Fontan procedure

ECHO = echocardiography; IAA = interrupted aortic arch; iESR = increased erythrocyte sedimentation rate; IV = intravenous; PA = pulmonary atresia; PS = pulmonary stenosis; VSD = ventricular septal defect.

in conjunction with complete courses of antibiotic therapy targeted at specific organisms when known. Fifteen patients have known follow-up from the time of their operation to the present.

In general, patients with a central venous line in place, in whom bacteremia developed, underwent catheter removal. Furthermore, venous access was maintained through a peripheral site when possible. When required, new central lines were placed through a different site and antibiotics were continued. Adherence to this protocol cleared nearly all cases of central line sepsis. However, endocarditis did develop in 5 patients, presumably related to central venous lines. Their special circumstances are addressed elsewhere in this report.

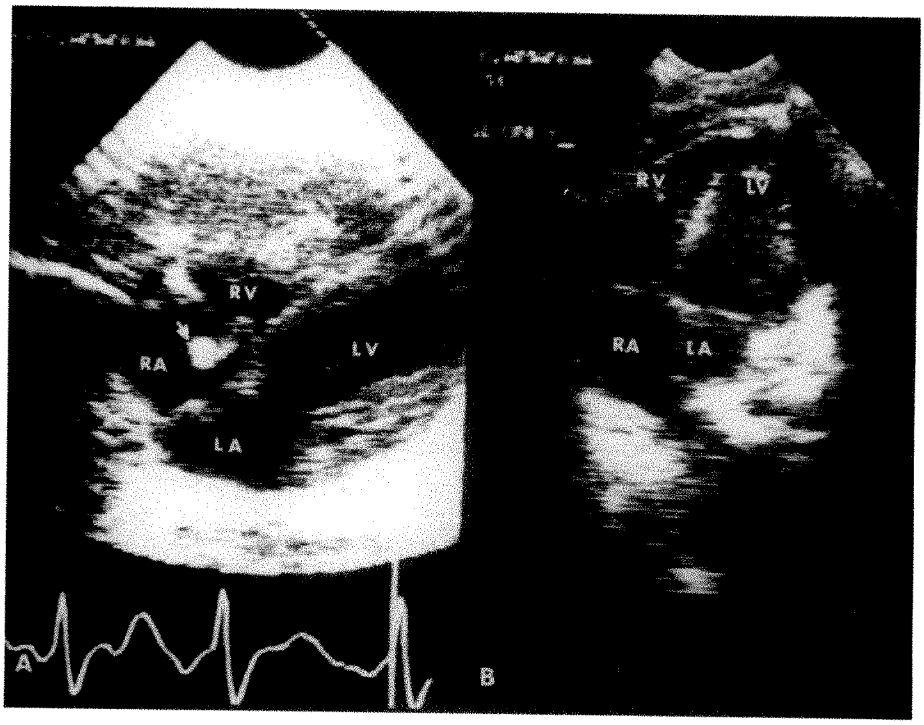


*Fig 1. (A) Apical preoperative echocardiogram showing echogenic mass (*arrow*) attached to septal leaflet of the tricuspid valve. (B) Postoperative echocardiogram showing absence of previously visualized mass related to septal leaflet of tricuspid valve. (*LA *= left atrium;* LV *= left ventricle;* RA *= right atrium;* RV *= right ventricle.)*

Results

Nineteen operations in 16 patients were performed for the treatment of endocarditis, as shown in Table 2. Three patients required a second operation. One had initial aortic valve replacement and pericardial exclusion of a subannular abscess. Persistent sepsis and a newly formed right ventricular vegetation resulted in the second operation for debridement. The patient died of arrhythmias and cardiac failure. The second patient with an unoperated ventricular septal defect had development of right ventricular and tricuspid vegetations and underwent debridement. Continued sepsis resulted in a second operation to debride recurrent vegetations on the tricuspid valve and pericardial ventricular septal defect closure. This was followed by complete recovery. Congestive failure developed in the third patient after aortic valve replacement for sepsis and was complicated by a left ventricular-to-right atrial fistula. The aortic valve was re-replaced and the fistula closed with pericardium and Dacron, which was followed by complete recovery [12].

Nine patients (56%) had previously identifiable cardiac disease. Six of these had previously undergone some type of corrective procedure. The other 3 of these had small unoperated ventricular septal defects (2) and preexisting rheumatic heart disease (1). Endocarditis developed in 5 patients (31%) as a result of indwelling central venous catheterization. Four of these were treated by removal of infected thrombus from the superior vena cava or right atrium only, and the other required a tricuspid valvuloplasty using pericardium for reconstruction. The remaining 2 patients had normal cardiac anatomy, but endocarditis developed from a remote extracardiac source. One of these was from a pneumococcal pneumonia, and the other from dental caries.

Table 2. Operations for Endocarditis

Procedure	No. of Operations[a]
Resection of vegetation (*a*)	7
Vegetation resection, VSD closure with pericardium (second operation for 1 of the patients in *a*)	1
Aortic valve replacement (No. 17 Björk-Shiley valve) (*b*)	1
Aortic valve replacement (No. 19 Björk-Shiley valve) and closure of left ventricular-to-right atrial fistula (second operation after *b*)	1
Aortic valve replacement (No. 19 St. Jude valve) and pericardial exclusion of subannular abscess (*c*)	1
Resection of right ventricular vegetation and debridement of outflow tract (second operation after *c*)	1
Mitral valve replacement (No. 27 Carpentier-Edwards porcine valve)	1
Tricuspid valve replacement (No. 1 Starr-Edwards, No. 27 Carpentier-Edwards porcine valve)	2
Closure of VSD	1
Excision of vegetation and septal leaflet of tricuspid valve, reconstruction with pericardium	1
Excision of vegetation from tricuspid valve and portion of papillary muscle	1
Removal of torn Eustachian valve and debridement of vegetations	1

[a] Nineteen operations were performed in 16 patients.

VSD = ventricular septal defect.

Table 3. Organisms Isolated From 16 Patients Who Underwent Operation for Endocarditis

Organism	Number	% Total
Staphylococcus aureus	3	19
Staphylococcus epidermidis	2	12.5
Haemophilus influenzae	2	12.5
Streptococcus pneumoniae	1	6
Gram-negative organisms (*Escherichia coli*, *Klebsiella*)	2	12.5
Candida species	2	12.5
None recovered	4	25

The organisms obtained by blood cultures or specimen cultures are listed in Table 3. No single organism was predominant. Four patients failed to grow an organism on culture but did have endocarditis based on clinical and operative findings.

There were four operative deaths in this series resulting in a 25% mortality (70% confidence limits, 13% to 40%). The only late death occurred 9 months after tricuspid valve replacement in a 16-year-old patient who died of congestive failure due to underlying cardiac disease (31% overall mortality; 70% confidence limits, 18% to 47%). Autopsy showed the prosthetic porcine valve to be intact, and there was no evidence of endocarditis. Three of the four perioperative deaths occurred in patients less than 2 years of age. Operative mortality rate in this age group was 43% compared with 11% in patients 2 years of age or older. Although the difference is striking, statistical significance was not achieved due to the small number of patients in the study. No single infecting organism or type of operation affected operative mortality.

Comment

The association of infective endocarditis and congenital heart disease has been well described [1, 2, 4–7]. Surgical treatment for endocarditis in children was initiated in 1940 by Touroff and Vesell [13], who reported successful recovery of a patient with endocarditis and patent ductus arteriosus after ligation. In 1961 Kay and associates [14] reported the cure of an adult patient with *Candida* endocarditis by ventricular septal defect closure and partial tricuspid valve excision. Four years later, Zakrzewski and Keith [2] described successful treatment of staphylococcal endocarditis after removal of the infected pledgets that were used to anchor the sutures after ventricular septal defect closure. Other authors have outlined guidelines and indications for surgical therapy in pediatric patients with endocarditis [5, 6]. The patients in our series under-

Table 4. Five Patients Requiring Resection of Vegetation Resulting From Central Venous Catheters

Patient No.	Age at Operation	Type of Catheter	Duration of Catheter Placement	Organism	Circumstances	Outcome
1	3 wk	ECMO cannulas ×2	6 d, 4 d	*S epidermidis* & group B *Streptococcus*	ECMO ×10 days; catheter change on day 6 for clots in circuit	Recovery
2	6 wk	1.9F Silastic	15 d	*Candida albicans*	28-wk gestation, NEC, laparotomy ×2; gram-negative sepsis	Died of MSOF
3	8 wk	1.9F Silastic	20 d	*S epidermidis*	27-wk gestation, hyaline membrane disease, hydrocephalus, parenteral nutrition	Recovery
4	4 mo	2.8F Silastic	13 d	*E coli, Klebsiella*	28-wk gestation, NEC, laparotomy; gram-negative sepsis	Died of MSOF
5	15 wk	2.7F Broviac	6 wk	*Candida tropicalis*	Acute lymphocytic leukemia, chemotherapy, leukopenia	Recovery

ECMO = extracorporeal membrane oxygenation; MSOF = multisystem organ failure; NEC = necrotizing enterocolitis.

went operations for indications that include: (1) persistent endocarditis and sepsis uncontrolled by antibiotic therapy, (2) threatened, embolized, or recurrent systemic embolization of vegetative material, and (3) cardiac decompensation, severe congestive heart failure, and cardiac arrhythmias due to myocardial structural damage.

The overall mortality in our series was 31%. One death occurred 9 months after tricuspid valve replacement in a 16-year-old boy. At autopsy the valve was without evidence of defect or infection and did not contribute to the patient's death. Of the four operative deaths, three occurred in patients less than 2 years of age. Johnson and Rhodes [1] have reported on the grave prognosis of children less than 2 years of age with endocarditis. Two of our patients were premature neonates with severe infections, and the third was a child with complex congenital heart lesions who had already undergone two previous corrective procedures. Half of the patients operated on for endocarditis in Schollin and associates' series died [6]. Schollin and associates note that surgical treatment may be necessary in a "few cases," and that it would be wise to consider operative intervention earlier as opposed to a last desperate effort, which is associated with a high operative mortality. Of the 9 patients greater than 2 years of age operated on for endocarditis in our series, there was only one death for an operative mortality rate of 11%. This trend toward a better outcome reflects a philosophy of early operative intervention for infection or heart failure when it becomes apparent that medical management alone will not be successful.

The spectrum of infective organisms included staphylococcal species as well as pneumococcal, gram-negative rods, and fungal species. This is similar to that found by other authors [1, 3, 5, 7, 10] who report staphylococcal or streptococcal species as those most frequently encountered. One-fourth of our operated patients had negative blood cultures. This is higher than that reported in other series, which range from 3% to 13% [1, 3, 7, 10]. These cases of endocarditis were diagnosed based on clinical, echocardiographic, and operative findings, and all patients had received lengthy courses of antibiotics before operative intervention.

Five patients (34%) with otherwise normal hearts had development of endocarditis as a complication of central line sepsis. These cases are outlined in Table 4. One patient, a 15-week-old girl with leukemia, had a long-term implantable catheter in place for chemotherapy administration. While she was immunocompromised as a result of chemotherapy, fungal endocarditis developed, which did not resolve after catheter removal and amphotericin-B therapy. She made a complete recovery after vegetation excision. Another patient was a neonate with group B *Streptococcus* sepsis, who required extracorporeal membrane oxygenation for 10 days. The extracorporeal membrane oxygenator venous cannula had to be changed on day 6 due to clots in the circuit. This cannula manipulation is not common, but probably played a role in the development of this patient's endocarditis. This patient also did well after operative removal of his vegetation.

The remaining three catheter-related infections were in premature neonates, who had soft Silastic (Ethicon, Somerville, NJ) catheters placed through basilic arm veins. All had other complications of prematurity including necrotizing enterocolitis, hyaline membrane disease, or hydrocephalus. Despite catheter removal and antibiotic therapy, endocarditis with vegetations developed. Two of these patients died postoperatively of sepsis and multisystem organ failure due to gram-negative and fungal organisms. The presence of a central venous catheter may have contributed to, but was not primarily responsible for, their septic condition. In the third patient, endocarditis was due to *Staphylococcus epidermidis*, probably related to the central line itself. Operative excision of the vegetation was required and this patient recovered. The two fatalities in this group were in patients whose sepsis was primarily either abdominal or pulmonary, and removal of their vegetations did not resolve the focus of infection.

Endocarditis due to central line sepsis has not been noted frequently in other series [3, 5], but accounted for one-third of the cases in ours. With the advent of neonatal and pediatric intensive care units, central venous catheterization for the delivery of fluids, medications, and nutrition has become more commonplace. This problem is certain to be encountered more frequently as the use of central lines in very young infants continues to grow [15–17].

Intracardiac vegetations associated with active infection represent a serious management problem due to persistent sepsis, myocardial structural damage, and threat of embolization. Appropriate antibiotic therapy may control the septic episode and even result in vegetation resolution, as was the case in 3 of our medically treated patients (see Table 1). Under these circumstances, the threat of embolization after sepsis resolution must be weighed against the morbidity and mortality of an open heart procedure to remove the vegetation. The decision to operate is much easier when intracardiac vegetations are associated with persistent sepsis despite antibiotic therapy.

A conservative operation, such as the excision of vegetations alone, may be all that is required to effect sterilization of the bloodstream. We performed seven such procedures for ongoing sepsis with demonstrable vegetations by echocardiogram (see Fig 1) that were unresponsive to antibiotic therapy alone. Karl and associates [4] reported 3 patients requiring vegetation excision who failed medical therapy. Vegetations form through the deposition of platelets and fibrin on injured vascular endothelium. Endocarditis ensues when circulating bacteria colonize a thrombotic vegetation. Growth of the vegetation continues through further deposition of platelets and fibrin, isolating the bacteria from neutrophils and antibiotics in the bloodstream. This phenomenon of protecting bacteria from phagocytosis has been termed a "zone of agranulocytosis" [3] and is one reason why a long duration of intravenous antibiotics is indicated for the eradication of organisms on infected vegetations. Operative debridement of vegetations results in near-complete eradication of the infected focus in the bloodstream, allowing antibiotics and phagocytosis to complete the sterilization process. Patients with persistent sepsis, candidemia, systemic emboli, and vegetations demonstrated by echocardiography should be considered candidates for vegetation excision.

Larger operations are frequently needed to properly clear the focus of infection and correct any associated hemodynamic problems. These may range from valve replacement to more complex reconstructive procedures. Several reports in the adult literature have showed that, although not desirable, it is possible to replace infected cardiac valves in the presence of bacteremia as long as adequate debridement of the valvular annulus is performed [18–20]. In general, we prefer to implant prosthetic heart valves for infective endocarditis unless other pressing indications call for a porcine or homograft valve. In our series, 5 patients had six valve replacements, of which four were prosthetic and two were porcine. Five of the native valves grew various microorganisms. There was one death, in a 10-year-old boy who, after aortic valve replacement with debridement of a subannular abscess, required a second operation for debridement of a right ventricular vegetation. Valve cultures were positive for *S aureus*, although he died of persistent congestive failure and cardiac arrhythmias rather than sepsis. The remaining patients all cleared their bacteremias after valve replacement. These data support the published conclusions that valve replacement or other reconstructive procedures are safe and efficacious in patients with ongoing bacteremia from a cardiac source [19, 20].

A selected number of cases involving valvular lesions may be treated with a more conservative resection and reconstruction rather than total valve replacement. Yee and Ullyot [21] reported good results in treating right-sided lesions in adults by partial valve resection and or defect repair using a pericardial patch. Initial insufficiency after valvuloplasty on right-sided valves is well tolerated and usually improves over time. We obtained good results in 1 patient who underwent excision of vegetation and the septal leaflet of the tricuspid valve, using pericardium for reconstruction. Two other patients had excisions of chorda or portions of papillary muscle of the tricuspid valve with good results. We used pericardium as an autologous tissue patch for valvular reconstruction and additionally for closure of ventricular septal defects, closure of an intracardiac fistula, and for the exclusion of a subannular abscess cavity from the left ventricle.

In summary, we report our experience with operative procedures used to treat endocarditis in children. Early operation before the onset of major hemodynamic problems should be practiced. Conservative resection of vegetations or valvuloplasty may provide adequate treatment. Pericardium provides an autologous tissue patch that is useful for repair of intracardiac and valvular defects.

References

1. Johnson CM, Rhodes KH. Pediatric endocarditis. Mayo Clin Proc 1982;57:86–94.
2. Zakrzewski T, Keith JD. Bacterial endocarditis in infants and children. J Pediatr 1965;67:1179–93.
3. King K, Harkness JL. Infective endocarditis in the 1980s. Part 1. Aetiology and diagnosis. Med J Aust 1986;144:536–40.
4. Karl T, Wensley D, Stark J, de Leval M, Rees P, Taylor JFN. Infective endocarditis in children with congenital heart disease: comparison of selected features in patients with surgical correction or palliation and those without. Br Heart J 1987;58:57–65.
5. Schollin J, Bjarke B, Wesström G. Infective endocarditis in Swedish children. I. Incidence, etiology, underlying factors and port of entry of infection. Acta Paediatr Scand 1986;75:993–8.
6. Schollin J, Bjarke B, Wesström G. Infective endocarditis in Swedish children. II. Location, major complications, laboratory findings, delay of treatment, treatment and outcome. Acta Paediatr Scand 1986;75:999–1004.

7. Johnson DH, Rosenthal A, Nadas AS. A forty-year review of bacterial endocarditis in infancy and childhood. Circulation 1975;51:581–8.
8. Cutler JG, Ongley PA, Shwachman H, Massell BF, Nadas AS. Bacterial endocarditis in children with heart disease. Pediatrics 1958;22:706–13.
9. Johnson DH, Rosenthal A, Nadas AS. Bacterial endocarditis in children under 2 years of age. Am J Dis Child 1975;129: 183–6.
10. Sholler GF, Hawker RE, Celermajer JM. Infective endocarditis in childhood. Pediatr Cardiol 1986;6:183–6.
11. Macaulay D. Acute endocarditis in infancy and early childhood. Am J Dis Child 1954;88:715–31.
12. Mavroudis C, Wampler J, Hodsden JE, Rees AH, Solinger RE, Elbl F. Modified aortoseptoplasty for anular abscess and erosion of the membranous septum. Chest 1984;85:442–4.
13. Touroff ASW, Vesell H. Subacute *Streptococcus viridans* endarteritis complicating patent ductus arteriosus. JAMA 1940;115: 1270–2.
14. Kay JH, Bernstein S, Feinstein D, Biddle M. Surgical cure of *Candida albicans* endocarditis with open-heart surgery. N Engl J Med 1961;264:907–10.
15. McGuinness GA, Schieken RM, Maguire GF. Endocarditis in the newborn. Am J Dis Child 1980;134:577–80.
16. Oelberg DG, Fisher DJ, Gross DM, Denson SE, Adcock EW III. Endocarditis in high risk neonates. Pediatrics 1983;71: 392–7.
17. Blieden LC, Morehead RR, Burke B, Kaplan EL. Bacterial endocarditis in the neonate. Am J Dis Child 1972;124:747–9.
18. Crosby IK, Carrell R, Reed WA. Operative management of valvular complications of bacterial endocarditis. J Thorac Cardiovasc Surg 1972;64:235–46.
19. Wilson WR, Danielson GK, Giuliani ER, Washington JA II, Jaumin PM, Geraci JE. Valve replacement in patients with active infective endocarditis. Circulation 1978;58:585–8.
20. Stinson EB, Griepp RB, Vosti K, Copeland JG, Shumway NE. Operative treatment of active endocarditis. J Thorac Cardiovasc Surg 1976;71:659–65.
21. Yee ES, Ullyot DJ. Reparative approach for right-sided endocarditis. Operative considerations and results of valvuloplasty. J Thorac Cardiovasc Surg 1988;96:133–40.

Left Ventricular Diverticulum With Hypertrophy of the Left Ventricular Apex

Chojiro Yamashita, MD, Hiroomi Nakamura, MD, Satoshi Tobe, MD,
Toshihiro Koterazawa, MD, and Sinnichirou Yamamoto, MD

Miki City Hospital and Department of Surgery, Division II, Kobe University School of Medicine, Kobe, Japan

A surgical case of diverticulum in the left ventricular apex is presented. A two-dimensional echocardiogram and magnetic resonance image showed a calcified tumor buried in the marked hypertrophied apex of the left ventricle. Enucleation of the oval and hard tumor (4 × 2.5 × 2.5 cm) was performed through the apex, and the defect was anastomosed by buttress sutures. Histologic examination demonstrated that the tumor cavity was filled with a thrombus encapsulated by thickened and calcified endocardium that extended to the left ventricular cavity. In this report, the etiology of the diverticulum with a hypertrophied myocardium is discussed.

(Ann Thorac Surg 1992;54:761–3)

Left ventricular diverticulum in adults is a very rare malformation. The majority of cases arise from the apex of the left ventricle and are usually found in children. In all cases, the muscular appendage extends outside the normal bounds of the heart and pericardium, and often extends through the diaphragm. In our case, the diverticulum was filled with a thrombus and buried in the hypertrophic myocardium of the left ventricular apex. We assume that our case was not a congenital anomaly but was caused by myocardial infarction due to apical hypertrophic cardiomyopathy.

A 58-year-old man was admitted to our hospital due to general fatigue and arrhythmia. Four years earlier, a ventricular premature beat and supraventricular capture were observed by a visiting doctor. Physical examination revealed normal vital signs except an irregular pulse. Cardiac and pulmonary auscultation revealed no cardiac murmur and vesicular breathing sounds. On chest roentgenogram, the cardiothoracic ratio was 0.43 and a rounded shadow 3 cm in diameter with calcification was found near the apex of the heart. An electrocardiogram showed atrial fibrillation and severe left ventricular hypertrophy with S-T segment depression in the lateral precordial lead. A two-dimensional echocardiogram revealed a low echoic lesion 2 cm in diameter in the apex and spade-like hypertrophy of the left ventricle. Magnetic resonance imaging demonstrated a spade-like hypertrophic myocardium and calcified tumor buried in the hypertrophic apex (Fig 1). A left ventricular angiogram showed a normal left ventricle and wall motion. Coronary angiography showed normal coronary arteries. The white blood cell count was 10.5×10^9/L with 16% eosinophils. Other laboratory examinations were within the normal limits. With a diagnosis of cardiac echinococcosis or a fibrous diverticulum, which has the risk of rupture, we proceeded to treat him surgically.

On January 7, 1991, operation was carried out through a median sternotomy. Fibrous adhesion was seen at the apex and was dissected. Malformation of the left ventricle was not found, but a hard tumor under the epicardium at the apex was detected by palpation. The epicardium was incised and the capsule was dissected from the myocardium (Fig 2). On the reverse side of the tumor, the capsule became a thin root and connected to the ventricular cavity. Cutting the root showed the capsule of the tumor to be fibrous endocardium, and the tumor was filled with thrombus. The left ventricular cavity showed moderate subendocardial fibrosis at the site of apical ventriculotomy. Near the apex, the myocardium was almost totally replaced by fibrous tissue. The defect was anastomosed with buttress sutures, reinforced by a felt strip (Fig 3). The schema of the tumor is showed in Figure 4. The postoperative course was uneventful. Histologic examination showed that the tumor was a thrombus encapsulated by fibrous endocardium with calcification.

Comment

Left ventricular diverticulum of the heart is a rare malformation. The majority arise from the apex of the left ventricle and are usually found in children. Only a few cases in adults have been reported. In the past, congenital aneurysm and diverticulum of the left ventricle were used synonymously. Treisman and associates [1] classified the defect as a diverticulum when its root of connection to the left ventricle was narrow and was associated with congenital midline lesions, and as an aneurysm if the connection was wide and there were no other congenital defects. Recently, the definition of a diverticulum is that its wall contains three cardiac layers (endocardium, myocardium, and pericardium) and it contracts normally. Mady and Paulo [2] stated that left ventricular diverticu-

---

Accepted for publication Dec 30, 1991.

Address reprint requests to Dr Yamashita, Department of Surgery, Division II, Kobe University School of Medicine, 7-5-2 Kusunoki cho Chuoku, Kobe, Japan 650.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

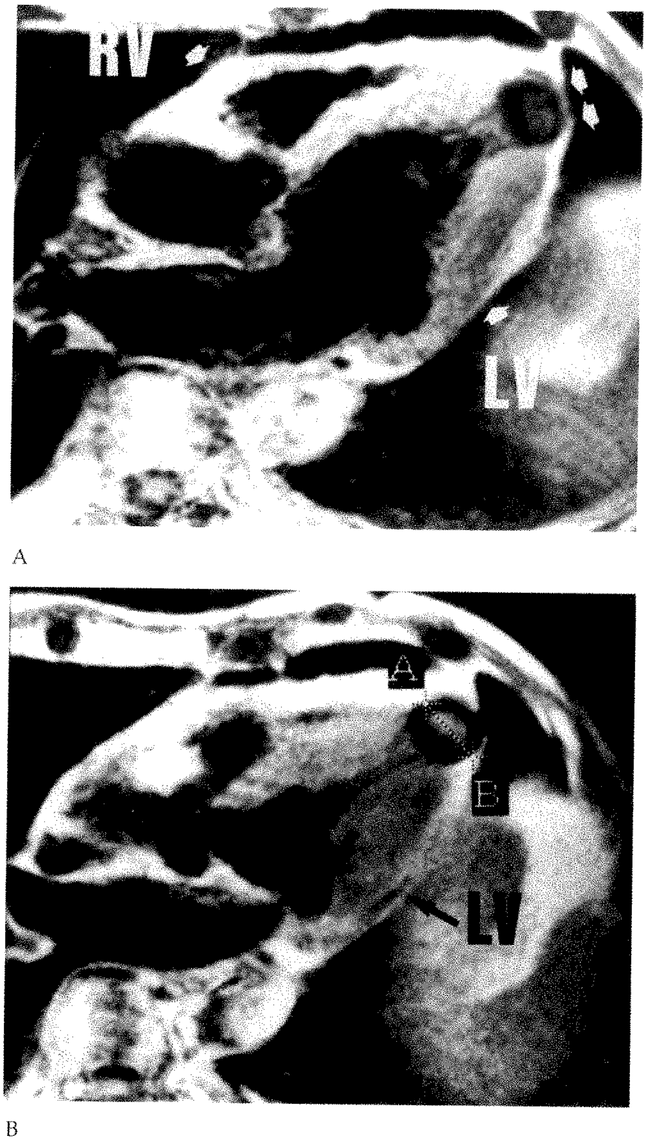


Fig 1. (A) Magnetic resonance imaging in diastole showed diverticulum buried in the hypertrophic myocardium of the left ventricle (LV). (B) Magnetic resonance imaging in systole showed diverticulum and a spade-like hypertrophic myocardium of the left ventricle. (RV = right ventricle.)

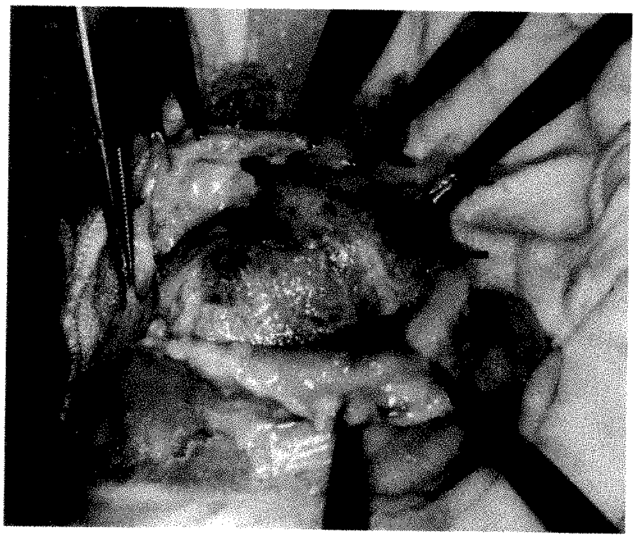


Fig 2. A tumor with a calcified capsule was dissected.

lum has two types; one is muscular and the other is fibrous. Muscular diverticulum is usually located at the apex or the inferoposterior wall. The wall of the muscular diverticulum consists of intact musle layers and some fibrous tissue. Fibrous diverticula are usually apical or subvalvular in position, and the walls are composed of fibrous tissue, with no contractility. An aneurysm of the left ventricle develops as a result of infection, ischemia, trauma, and postoperative coronary disease and consist of a fibrous saccular lesion with paradoxical contraction of its wall.

In our case, a tumor in the apex and hypertrophy of the left ventricle were discovered by echocardiogram. Magnetic resonance imaging provided valuable anatomical information about a mass buried in the hypertrophic myocardium of the left ventricle. The mass showed no contraction, so this tumor was initially thought to be echinococcosis or a fibrous diverticulum [3]. Shizukuda and associates [4] and Kida and co-workers [5] reported left ventricular diverticulum with hypertrophic cardiomyopathy. Tecklenberg and colleagues [6] reported that an obstructing hypertrophic mass localized in the midportion of the ventricle created a pressure gradient between the apical and basal portions. They assumed that the ventricular apex, chronically exposed to high intracavitary pressure, gradually changed to a dilated muscular chamber, or diverticulum, as the midventricular obstruction worsened [6]. In hypertrophic cardiomyopathy, angina pectoris occurs as the result of an imbalance between oxygen supply and demand as a consequence of the greatly increased myocardial mass. Transmural infarction may occur in the absence of narrowing of the extramural coronary arteries.

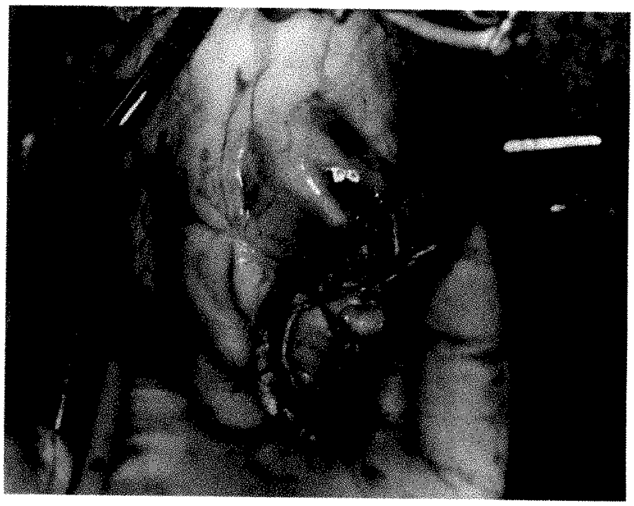


Fig 3. The defect was anastomosed by buttress sutures, as well as being reinforced by a felt strip.

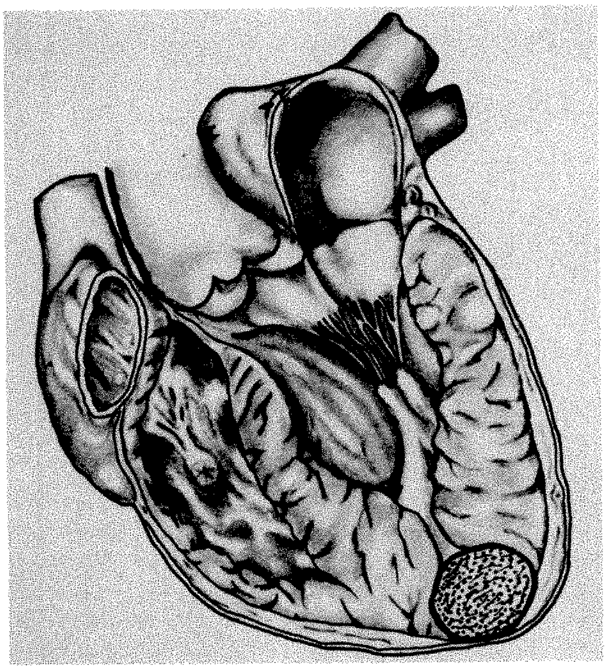


Fig 4. Schema of the tumor and hypertrophied myocardium.

Impaired diastolic relaxation may also produce subendocardial ischemia as a result of prolonged maintenance of wall tension with a concomitant slower than normal decrease in the impedance to coronary blood flow [7, 8].

In conclusion, we hypothesize that severe myocardial hypertrophy produced subendocardial and apical infarction, which eventually became diverticulum with a mural thrombus.

References

1. Treisman B, Cooley DA, Luftschanowski R, Leachman RD. Diverticulum or aneurysm of left ventricle. Am J Cardiol 1973;32:119–23.
2. Mady C, Paulo S. Left ventricular diverticulum: analysis of two operated cases and review of the literature. Angiology 1982;33:280–6
3. Tellez G, Nojek C, Juffe A, Rufilanchas J, O'Connor F, Figuera D. Cardiac echinococcosis: report of 3 cases and review of literature. Ann Thorac Surg 1976;21:425–30.
4. Shizukuda Y, Murakami H, Iwakura M, et al. Siblings with left ventricular diverticulum and hypertrophic cardiomyopathy. J Cardiol 1988;18:867–74.
5. Kida M, Hoshino T, Yokoyama S, et al. Left ventricular diverticulum with marked hypertrophy of the left ventricular apex revealed by thallium-201 myocardial emission CT: a case report. J Cardiol 1985;15:1263–74.
6. Tecklenberg LP, Alderman LE, Billingham EM, Shumway EN. Diverticulum of the left ventricle in hypertrophic cardiomyopathy. Am J Med 1978;64:707–14.
7. Braunwald E. Heart disease, a textbook of cardiovascular medicine. Philadelphia: W.B. Saunders, 1988:1418–30.
8. Macina G, Singh A, Drew TM, Moran JM, Most AS. Asymmetric myocardial hypertrophy, left ventricular aneurysm, mural thrombus, and sudden death. Am Heart J 1986;111: 175–8.

Chronic Fibrosing Mediastinitis and Superior Vena Caval Obstruction From Blastomycosis

Carl F. Lagerstrom, MD, Holly G. Mitchell, MD, Barney S. Graham, MD, PhD, and John W. Hammon, Jr, MD

Department of Cardiac and Thoracic Surgery and Division of Infectious Diseases, Department of Internal Medicine, Vanderbilt University, Nashville, Tennessee

Chronic fibrosing mediastinitis is most commonly a complication of granulomatous disease caused by histoplasmosis. We report a case of *Blastomyces dermatitidis* causing superior vena caval obstruction from fibrosing mediastinitis.

(Ann Thorac Surg 1992;54:764–5)

There are a number of clinical syndromes caused by invasion and compression of mediastinal structures secondary to granulomatous disease. The characteristic dense, fibrous mass may involve the pericardium, esophagus, tracheobronchial structures, or the central venous circulation, which accounts for the wide spectrum of clinical presentations. An etiologic organism is often not identified; however, histoplasmosis, tuberculosis, and nocardiosis have been described [1, 2]. A case of chronic fibrosing mediastinitis from *Blastomyces dermatitidis* is reported.

A 66-year-old woman was in her usual state of good health until 1 year before referral, when she noticed left shoulder and arm pain and swelling. She was diagnosed as having deep venous thrombosis of the axillary and brachial veins. The patient was hospitalized for intravenous heparin therapy, and her symptoms resolved. She was subsequently discharged on a regimen of warfarin (5 mg/day), doing well. After 6 months her anticoagulation therapy was discontinued, and the left arm pain and swelling returned. In addition, the swelling was now noted in her face and neck as well. A venogram was performed, showing superior vena caval occlusion due to compression from a soft tissue mass in the superior mediastinum. The warfarin therapy was reinstituted, and a magnetic resonance imaging study of the chest demonstrated a soft tissue density from below the sternal notch to the subcarinal region. Her symptoms did not improve, and at the time of referral she complained of facial, neck, and arm swelling and pain. She noted a 6.8-kg weight loss over the past year but had no other constitutional symptoms.

Her physical examination found her to be moderately obese with stable vital signs and no fever. She had moderate, diffuse facial and neck edema with jugular venous distention to 4 cm below the ear. Both upper extremities were edematous with no cyanosis or clubbing. The patient's laboratory studies were all normal.

She was taken to the operating room for exploration and biopsy of the mediastinal mass causing superior vena caval obstruction. A median sternotomy was performed, and numerous dilated venous collaterals were found beneath the sternum. Examination of the anterior mediastinum revealed an extremely hard, dense mass involving the entire anterior superior mediastinum in the area of the innominate vein. The innominate vein and superior vena cava were both involved and occluded by the mass. Numerous biopsy specimens were taken of the mass and submitted to pathologic examination. Dense fibrous reaction was seen on frozen section, and touch preparation revealed numerous fungal elements whose morphology was characteristic of blastomycosis (Fig 1). Because of the benign diagnosis, it was believed that a venous bypass should be constructed to relieve her superior vena caval obstruction. The entire saphenous vein was then harvested from the patient's left leg and bisected. The vein was wrapped around a 28F chest tube, and using a running 6-0 Prolene (Ethicon, Somerville, NJ) suture, a spiral vein graft was constructed by performing a suture line over the entire length of the vein. An anastomosis was performed using the spiral vein graft from the left internal jugular-subclavian vein confluence to the right atrium (Fig 2). There was good flow through the venous graft, which lay in the mediastinum in a fashion similar to the patient's innominate vein.

Postoperatively she had an uncomplicated course. Subsequent cultures from the mediastinal tissue grew *Blastomyces dermatitidis*. Serological studies showed antibody against *Blastomyces dermatitidis* by immunodiffusion, but were negative for antibody against *Histoplasma capsulatum*. Her facial swelling was noticeably improved; however, she still had some residual arm swelling. She was treated with warfarin sodium and ketoconazole, 400 mg twice per day for 6 months and 400 mg/day for an additional 6 months.

Comment

North American blastomycosis is a suppurative and granulomatous infection primarily affecting the skin and the lungs, although bones and the genitourinary tract may be affected. Infection begins in the lung after inhalation of

---

Accepted for publication Jan 6, 1992.

Address reprint requests to Dr Lagerstrom, Thoracic Surgery, TVC 2973, The Vanderbilt Clinic, Nashville, TN 37232.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

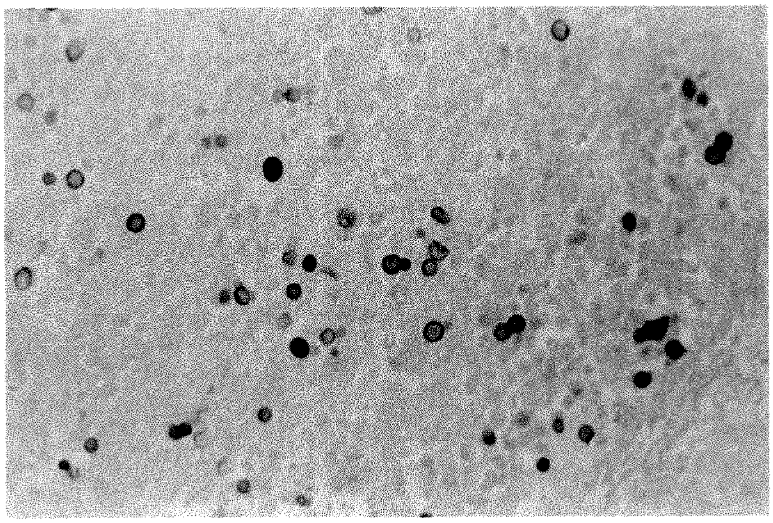


Fig 1. High-power view of numerous yeast forms within the tissue excised at operation. Note the broad-based budding at the center of the field, characteristic for blastomyces. (Gomori methamine silver; ×320 before 11% reduction.)

fungal conidia, which have a reservoir in soil. The skin lesions usually begin as papules that ulcerate and become chronic. Patients with pulmonary involvement may present with a cough productive of mucoid sputum, chest pain, hemoptysis, mild fever, or malaise [3].

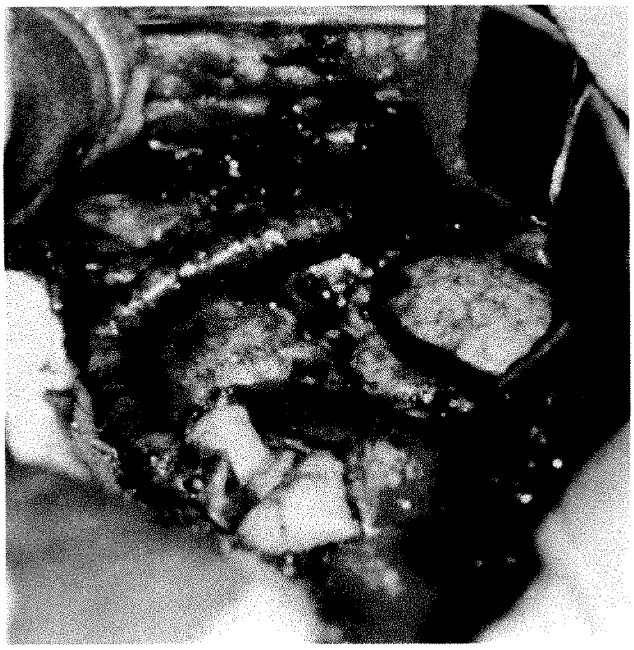


Fig 2. Spiral vein graft in situ.

In the present case, chronic fibrosing mediastinitis was due to *Blastomyces dermatitidis*. As reported in previous series, an etiologic organism or agent may not always be found for chronic fibrosing mediastinitis [1, 2]. In our case, the diagnosis was readily made as both the touch preparation slides and cultures from the biopsy material demonstrated extensive infiltration by blastomycosis. A spiral vein graft as described by Doty [4] was used to alleviate her symptoms of superior vena caval obstruction. The medical treatment for chronic mediastinitis secondary to blastomycosis is problematic, because the condition is so rare. However, because of the difficulty of long-term venous access for the administration of amphotericin B, ketoconazole was used for therapy based on its reported efficacy [5].

References

1. Dunn EJ, Ulicny KS, Wright CB, Gottesman L. Surgical implications of sclerosing mediastinitis: a report of six cases and review of the literature. Chest 1990;97:338–46.
2. Schowengerdt CG, Suyemato R, Main FB. Granulomatous and fibrous mediastinitis: a review and analysis of 180 cases. J Thorac Cardiovasc Surg 1969;57:365–79.
3. Takaro T. Thoracic and actinomycetic and mycotic infections. In: Shields TW, ed. General thoracic surgery. 3rd ed. Philadelphia: Lea & Febiger, 1989:809–11.
4. Doty DB. Bypass of superior vena cava: six years' experience with spiral vein graft for obstruction of superior vena cava due to benign and malignant disease. J Thorac Cardiovasc Surg 1982;83:326–38.
5. McManus EJ, Jones JM. The use of ketoconazole in the treatment of blastomycosis. Am Rev Respir Dis 1986;133:141–3.

Saphenous Vein Graft Pseudoaneurysm Formation After Postoperative Mediastinitis

Julian A. Smith, FRACS, and Jacob Goldstein, FRACS

Cardiothoracic Surgery Unit, Alfred Hospital, Prahran, Victoria, Australia

Pseudoaneurysm formation involving the body of an aortocoronary saphenous vein graft is a rare event. True aneurysmal dilatation of the graft and anastomotic pseudoaneurysm formation occur more commonly. We present the case of a 73-year-old woman in whom a pseudoaneurysm communicating with the body of a posterior descending coronary artery saphenous vein graft developed, presumably after a postoperative sternal wound infection. The aneurysm was excised and the defect within the saphenous vein graft repaired using hypothermia and circulatory arrest.

(Ann Thorac Surg 1992;54:766–8)

Postoperative mediastinal infection is a serious complication of myocardial revascularization. A potentially lethal sequel of mediastinal sepsis is pseudoaneurysm formation. This may occur at a variety of positions including anastomoses and cannulation sites, but very rarely within the body of a saphenous vein graft alone. We report the case of pseudoaneurysm formation involving an aortocoronary saphenous vein graft, presumably after an episode of mediastinal sepsis.

A 73-year-old non–insulin-dependent diabetic woman with postinfarction angina pectoris due to triple-vessel coronary disease underwent coronary artery bypass grafting in early April 1991. Her left internal mammary artery was applied to the left anterior descending coronary artery, and separate reversed saphenous vein grafts were applied to the obtuse marginal and posterior descending coronary arteries.

Her initial postoperative course was uncomplicated until she presented in early May 1991 with a septicemic illness due to *Staphylococcus aureus* and renal failure. A small hemoserous discharge was noted from the lower end of her sternal wound. The wound was not tender and the bone edges were firmly united. The lower end of her wound was explored and no evidence of deep-seated infection was found. She was treated with intravenous antibiotics, rehydration, and dopamine for her renal failure and made a satisfactory recovery.

In the middle of June 1991 she was seen again with an enlarging, pulsatile mass over the xiphoid region. A lateral chest roentgenogram (Fig 1) revealed her lower figure-of-8 sternal wire was displaced anteriorly from the body of the sternum. Needle aspiration of the mass revealed bloody fluid from which *Staphylococcus aureus* was grown. Echocardiography confirmed the presence of a cavity that communicated with the circulation.

She underwent an emergency operation with cardiopulmonary bypass being established through an arterial cannula in the femoral artery and venous cannulas within the femoral and internal jugular veins. After cooling to 18°C, during which ventricular fibrillation occurred, the circulation was turned off and the mass entered. A bilobar aneurysm cavity containing blood was found (Fig 2). The superficial portion was approximately 8 × 5 cm in size with its neck at the level of the sternum, which had been eroded above the xiphoid. The lower, slightly smaller portion lay below sternal level, but above the heart. There was a bleeding vessel within the deepest portion, which represented erosion of the saphenous vein graft feeding the posterior descending coronary artery. The lowest (most inferior) sternal wire lay almost free within the anterior cavity but was still attached to a remnant of sternum at one point.

Surrounding the cavity, but slightly superiorly, around the middle sternal wire was a collection of purulent material which drained from around this wire and multiple lateral sinuses within the soft tissues of the chest wall. There was much necrotic tissue surrounding both the aneurysm cavity and the purulent material, with the skin over the point of the aneurysm cavity breaking down. The upper half of the sternum was intact, with no evidence of infection.

The wall of the aneurysm cavity was removed and the bleeding saphenous vein graft in the base of the cavity was oversewn with 5-0 Prolene (Ethicon, Somerville, NJ) suture. All necrotic and purulent material was debrided and sections of sternum and costal cartilages were excised to leave freely bleeding surfaces. The patient was rewarmed, spontaneously defibrillated, and weaned from cardiopulmonary bypass with ease. The resultant sternal cavity was dressed with povidone-iodine (Betadine; Faulding Pharmaceuticals, South Australia)–soaked gauze.

After the use of regular dressings and systemic antibiotics to eradicate local sepsis, the sternal defect was repaired by rotating a right pectoralis major muscle flap. However, the resultant wound broke down and she required the transfer of omentum and a split skin graft to close the defect. She was discharged home well in the

---

Accepted for publication Jan 9, 1992.

Address reprint requests to Dr Goldstein, Cabrini Medical Center, Private Consulting Rooms, Isabella Street, Malvern, 3144 Victoria, Australia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

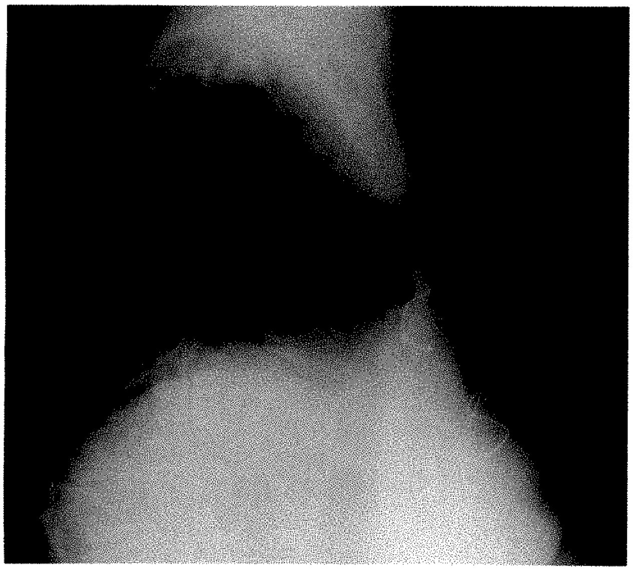


Fig 1. Lateral chest roentgenogram showing the anteriorly displaced inferior sternal wire.

middle of August 1991. The final reconstructive result is shown in Figure 3.

Comment

The most common form of aneurysms seen in saphenous vein aortocoronary grafts are the true atherosclerotic variety [1, 2]. Their incidence increases with time and they are often filled with thrombus, thus contributing to late graft stenosis and occlusion. False or pseudoaneurysm formation is rare and may occur at proximal [3] or distal [4] anastomotic sites. Mediastinal sepsis, especially due to *Staphylococcus aureus*, is the major predisposing factor in more than half of the cases [3]. Mycotic or infected pseudoaneurysms result from direct extension or hematogenous seeding to the anastomotic site leading to suture line dehiscence. Involvement of the body of the graft in this process is unusual, but mycotic aneurysm formation at this location has been reported to coexist with an anastomotic pseudoaneurysm [5]. Presumably the body of the graft or a branch ligature is directly invaded.

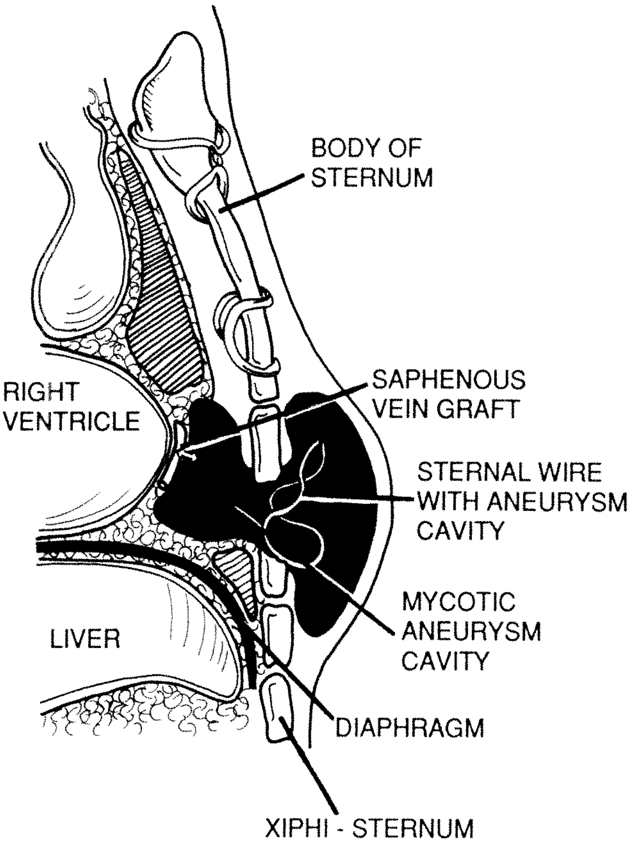


Fig 2. Midsagittal section diagram showing the operative findings (see text).

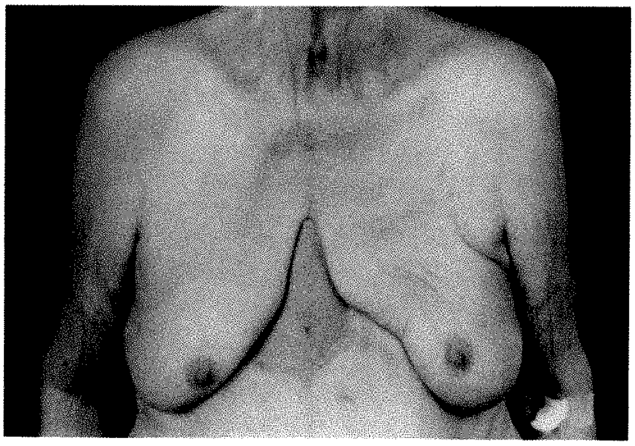


Fig 3. Completed chest wall reconstruction after filling the defect with omentum and laying on a split skin graft.

It is clear that our patient had deep-seated mediastinal sepsis that was not apparent at her original presentation. The diagnosis of these aneurysms may be difficult [3]. The symptoms may include fever, chest pain, evidence of myocardial ischemia, local compressive features, or rupture [3, 6]. We were aided by the extension of the process to the surface. Echocardiography was an ideal noninvasive means of confirming the diagnosis. Other investigations that have been employed include contrast-enhanced computed tomography, magnetic resonance imaging, and angiography [3, 7].

As the risk of rupture is high, expeditious surgical repair is required, although successful transcatheter embolization has been reported [8]. We, along with others [3, 9, 10], recommend the use of cardiopulmonary bypass, deep hypothermia, and a brief period of circulatory arrest to achieve a safe re-entry, aneurysm excision, and repair. It was impossible to primarily close the wound in our patient, and therefore subsequent soft tissue reconstruction was required. A long course of appropriate antibiotics is mandatory in these patients.

We have presented a rare sequel to the complication of mediastinal sepsis after coronary artery bypass grafting. The involvement of the body of the saphenous vein graft and the subsequent presentation were most unusual. A successful outcome was achieved by using a stepwise management plan.

We acknowledge the assistance of Richard Maxwell, FRACS, and Roger Wale, FRACS, in managing this patient.

References

1. Neitzel GF, Barboriak JJ, Pintar K, Qureshi I. Atherosclerosis in aortocoronary bypass grafts. Morphological study and risk factor analysis 6 to 12 years after surgery. Arteriosclerosis 1986;6:594–600.
2. Pintar K, Barboriak JJ, Johnson WD, Co ED. Atherosclerotic aneurysm in aortocoronary vein graft. Arch Pathol Lab Med 1978;102:287–8.
3. Sullivan KL, Steiner RM, Smullens SN, Griska L, Meister SG. Pseudoaneurysm of the ascending aorta following cardiac surgery. Chest 1988;93:138–43.
4. De Haan HPJ, Huysmans HA, Weeda HWH, Bosker HA, Buis B. Anastomotic pseudoaneurysm after aorto-coronary bypass grafting. Thorac Cardiovasc Surg 1985;33:55–6.
5. Douglas BP, Bulkley BH, Hutchins GM. Infected saphenous vein coronary artery bypass graft with mycotic aneurysm. Fatal dehiscence of the proximal anastomosis. Chest 1979;75:76–7.
6. Rosin MD, Ridley PD, Maxwell PH. Rupture of a pseudoaneurysm of a saphenous vein coronary arterial bypass graft presenting with superior caval venous obstruction. Int J Cardiol 1989;25:121–3.
7. Sherry CS, Harms SE. MR imaging of pseudoaneurysms in aortocoronary bypass graft. J Comput Assist Tomogr 1989;13:426–9.
8. Kim D, Guthaner DF, Wexler L. Transcatheter embolization of a leaking pseudoaneurysm of saphenous vein aortocoronary bypass graft. Cathet Cardiovasc Diagn 1983;9:591–4.
9. Lillehei CW, Todd DB, Levy MJ, Ellis RJ. Partial cardiopulmonary bypass, hypothermia, and total circulatory arrest. A lifesaving technique for ruptured mycotic aortic aneurysms, ruptured left ventricle, and other complicated cardiac pathology. J Thorac Cardiovasc Surg 1969;58:530–44.
10. Smith P, Qureshi S, Yacoub MH. Dehiscence of infected aortocoronary vein graft suture lines. Cause of late pseudoaneurysm of ascending aorta. Br Heart J 1983;50:193–5.

Unusual Complication of Temporary Pacing Wires in Children

Joe W. R. Bolton, MD, and John E. Mayer, Jr, MD

Department of Cardiothoracic Surgery, Boston University Medical Center, and Department of Cardiac Surgery, Children's Hospital, Boston, Massachusetts

There have been numerous complications described concerning temporary epicardial pacing wires including infection, bleeding, and coronary artery graft disruption. We report a case in which the heart was ensnared by the pacing wire, resulting in cardiac decompensation during attempted removal. This complication may be avoided by assuring that a smaller loop of pacing wire remains in the pericardium.

(Ann Thorac Surg 1992;54:769–70)

The patient is a 3½-year-old boy who had previously had Gore-Tex patch repair of coarctation of the aorta and subsequent development of subaortic stenosis (gradient, 55 mm Hg). On his second hospital day he was taken to the operating room, where he underwent resection of a subaortic membrane 2 mm below the valve and extending between the right coronary and noncoronary cusps. This was accompanied by septal myectomy. The operation was uneventful, and he was in sinus rhythm postoperatively.

A left atrial catheter was placed for monitoring purposes along with a single right ventricular temporary epicardial pacing wire and a single mediastinal chest tube. A loop of pacemaker wire was left along the diaphragmatic surface of the right ventricle.

The left atrial catheter was removed on the first postoperative day and the mediastinal tube was removed on the second postoperative day. The remainder of his recovery was uncomplicated until the day before his planned discharge (postoperative day 3) when he was to have his pacing wire removed.

While we were attempting to remove the ventricular pacing wire, the wire broke above the skin level and the child became unresponsive, cyanotic, bradycardiac, and hypotensive to the point of requiring chest compressions to maintain perfusion. He spontaneously recovered normal sinus rhythm with normal blood pressure (110 mm Hg/palpable) and became fully responsive. Because there were no physical findings suggestive of tamponade a second attempt was made to try to remove the remainder of the pacing wire. With slow, steady pressure the wire was withdrawn about 10 cm at which time the child again became unresponsive and cyanotic. His heart rate decreased from 142 to 72 beats/min and there was loss of a palpable pulse. Again chest compressions and airway management were instituted. Atropine was given without result, followed by epinephrine. Again, within minutes the child spontaneously recovered. An echocardiogram at the time revealed no evidence of tamponade and the child was transferred to the intensive care unit.

An anteroposterior and lateral chest roentgenogram performed immediately after the event had findings suggesting that a loop of pacing wire had migrated cephalad, encircling the heart (Figs 1, 2). Based on these findings the child was taken to the fluoroscopy suite, where the wire was removed without further difficulty. The child was discharged to home on the fifth postoperative day.

Comment

Temporary pacing wires are routinely used after pediatric as well as adult cardiac operations. These wires may be beneficial in both diagnosis and treatment of cardiac dysrhythmias after cardiac operations; however, they are not without complications. One report noted a complication rate in an adult population of 0.4%, which fell to 0.09% after a modification of the insertion technique [1].

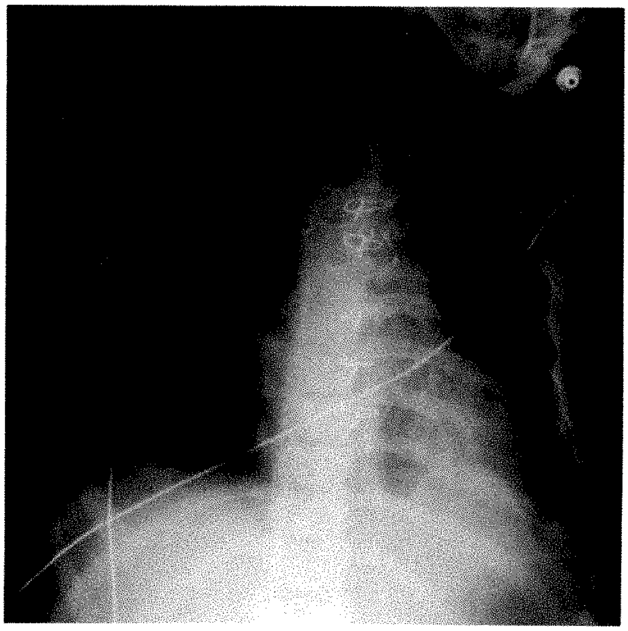


Fig 1. Anteroposterior chest roentgenogram after epicardial wire manipulation.

Accepted for publication Jan 13, 1992.

Address reprint requests to Dr Bolton, Department of Cardiothoracic Surgery, Boston University Medical Center, 88 E Newton St, Boston, MA 02118.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

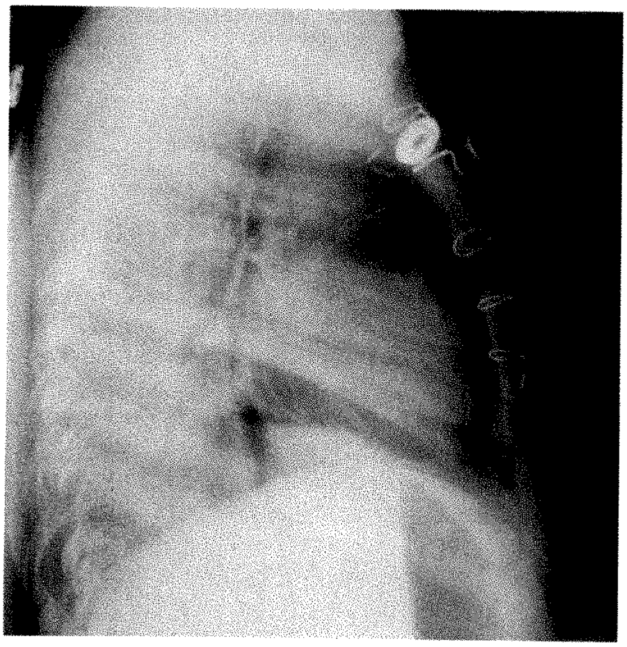


Fig 2. Lateral chest roentgenogram after epicardial wire manipulation.

Although there are numerous complications described concerning temporary epicardial pacing wires including bleeding, infection, coronary artery graft disruption, failure of sensing or pacing, and inability to remove the wire, it is very unusual for the heart to be ensnared by a wire and result in cardiac decompensation. We theorize that the redundant loop of wire left in the pericardium at its placement was large enough to allow migration around the apex of the heart. The tension exerted while the wire was removed either constricted the heart to the point that its cardiac output was seriously decreased or caused coronary artery compression leading to decreased perfusion and syncope. We believe that this complication may be avoided in the future by assuring that a smaller loop of pacing wire remains in the pericardium.

Reference

1. Del Nido P, Goldman BS. Temporary epicardial pacing after open heart surgery: complications and prevention. J Cardiac Surg 1989;4:99–103.

Aneurysm of Coronary Arteriovenous Fistula Presenting as a Calcified Mediastinal Mass

Yutaka Okita, MD, Shigehito Miki, MD, Kenji Kusuhara, MD, Yuichi Ueda, MD, Takafumi Tahata, MD, Tetsuro Sakai, MD, Akitoshi Tatsumi, MD, and Morihisa Kitano, MD

Departments of Cardiovascular Surgery and Thoracic Surgery, Tenri Hospital, Nara, Japan

A 61-year-old woman with a giant aneurysm of the coronary arterial fistula between the left anterior descending coronary artery and the main pulmonary artery underwent aneurysmal resection and closure of the fistula. This was a very unusual case with rare congenital malformation with secondary atherosclerotic change.

(Ann Thorac Surg 1992;54:771–3)

Communication between coronary arteries and the cardiac chambers is a rare type of congenital malformation [1, 2]. Aneurysmal formation of a coronary arteriovenous fistula is even more unusual [1, 3]. In this report, we describe a case of a giant aneurysm of the coronary arteriovenous fistula that presented as a calcified mediastinal mass.

A 61-year-old woman had an abnormal mediastinal shadow on chest roentgenogram. Twelve years earlier, she had been diagnosed as having hypertension and an abnormal mediastinal shadow on chest roentgenogram when she underwent hysterectomy. One month before admission, she underwent curative sigmoid colectomy for carcinoma of the sigmoid colon, and the abnormal chest shadow was noted to be enlarged compared with its size on the previous chest roentgenogram. She has had a continuous cardiac murmur since childhood and was thought to have a small patent ductus arteriosus. Physical examination revealed a grade 2/6 continuous cardiac murmur without thrill. Blood pressure was 142/98 mm Hg. Chest roentgenogram showed a normal-sized cardiac shadow (cardiothoracic ratio, 0.46) with a prominent aortic knob. Two oval calcified shadows were detected at the left cardiac border (Fig 1). Electrocardiogram was normal except for mildly high voltage of the R wave at the left precordial leads. Two-dimensional echocardiography did not reveal any intracardiac or extracardiac abnormalities. Magnetic resonance imaging (Fig 2) showed a round cystic lesion located in the left of the right ventricular outflow tract and in front of the left coronary artery. Radiocardiogram revealed a normal cardiac index of 3.80 $L \cdot min^{-1} \cdot m^{-2}$ but failed to demonstrate any intracardiac shunt. Neither cardiac catheterization nor angiocardiography was performed. A diagnosis of dermoid cystic tumor of the anterior mediastinum was made.

At operation, an egg-shaped elastic cardiac tumor 5 cm in diameter was found between the right ventricular outflow tract and left anterior descending coronary artery. There were three dilated communicating vessels from the left anterior descending coronary artery to the tumor. Another smaller (1.5 cm) solid tumor was adjacent and cephalad to the main tumor. Many tortuous vessels arising from the tumor were observed anterior to the main pulmonary artery (Fig 3). The right coronary artery was normal. The intraoperative direct epicardial echocardiography demonstrated that the bloodstream was arising from left anterior coronary artery, running through the tumor and tortuous vessels, and flowing into the main pulmonary artery. The correct diagnosis of arteriovenous fistula from the left anterior descending artery to the main pulmonary artery with aneurysmal formation was established. Using cardiopulmonary bypass with moderate systemic hypothermia, the aneurysms were resected, and the afferent and efferent vessels were individually di-

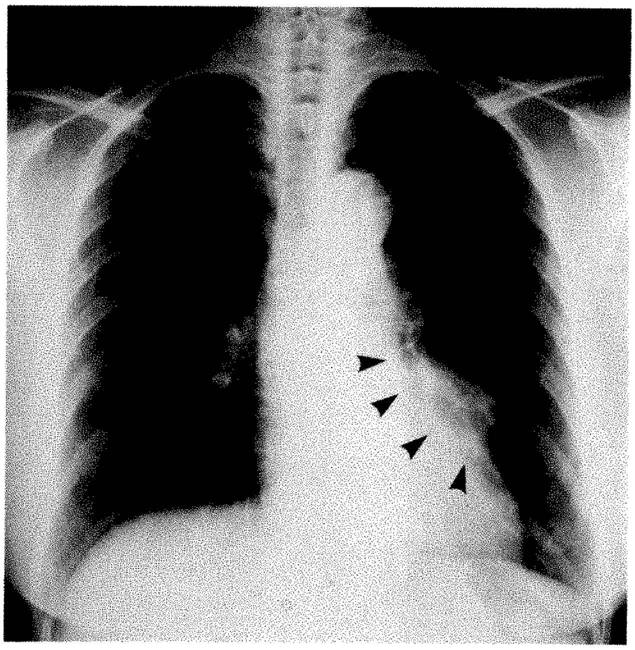


Fig 1. Preoperative plain chest roentgenogram. Arrow heads *point out the calcified mass.*

Accepted for publication Jan 14, 1992.

Address reprint requests to Dr Okita, Department of Cardiovascular Surgery, Tenri Hospital, 200 Mishima, Tenri, Nara 632, Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

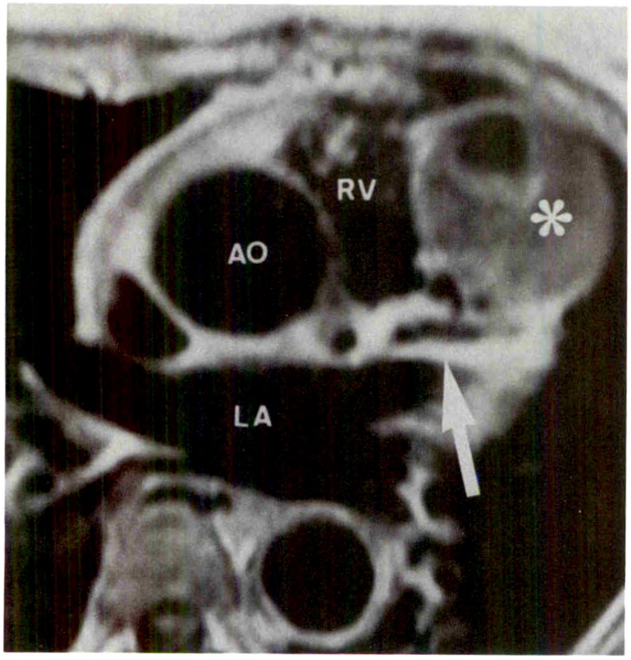


Fig 2. Magnetic resonance imaging. (AO = *ascending aorta;* arrow = *left coronary artery;* asterisk = *cystic mass;* LA = *left atrium;* RV = *right ventricular outflow tract.)*

vided. The aneurysmal wall was calcified, and laminated thrombi occupied nearly the entire cavity. Histological study of the aneurysmal wall revealed severe atherosclerotic changes. The postoperative course was uneventful, and the continuous cardiac murmur has disappeared.

Comment

Coronary arteriovenous fistulas are rare; they were identified in only 0.2% of routine cardiac angiographic studies conducted over a 10-year period [1], and are usually congenital. Aneurysms are more common than fistulas, having been found in from 0.3% to 4.5% of routine cardiac angiographic studies, and are usually acquired [4, 5]. In more than half of these, coronary arterial aneurysms are secondary to atherosclerosis; such aneurysms occur predominantly in aged men. The second most frequent cause of coronary arterial aneurysms is systemic vasculitis, such as systemic lupus erythematosus, Takayasu's arteritis, or Kawasaki's disease [5]. In some reported coronary arterial aneurysms and fistulas there have been histologic features suggestive of arterial dysplasia [2, 6]. Edwards [6] has noted that aneurysms occur proximal to arteriovenous fistulas and may be secondary to atherosclerosis. Aneurysms associated with coronary artery fistulas arise more commonly from the right coronary artery (55%) than the left (35%); in 5% of the cases they are bilateral [1–3]. Among 58 patients reported by Urrutia and associates [7], multiple fistulas were identified in 16%, an angiomatous lesion in 10%, and aneurysmal fistula in 19%. However, giant aneurysm of the coronary arterial fistula that developed in fistulous vessels and not in the coronary artery proximal to the fistula is considered to be exceedingly rare. In 1947, Bjork and Crafoord [8] reported the first

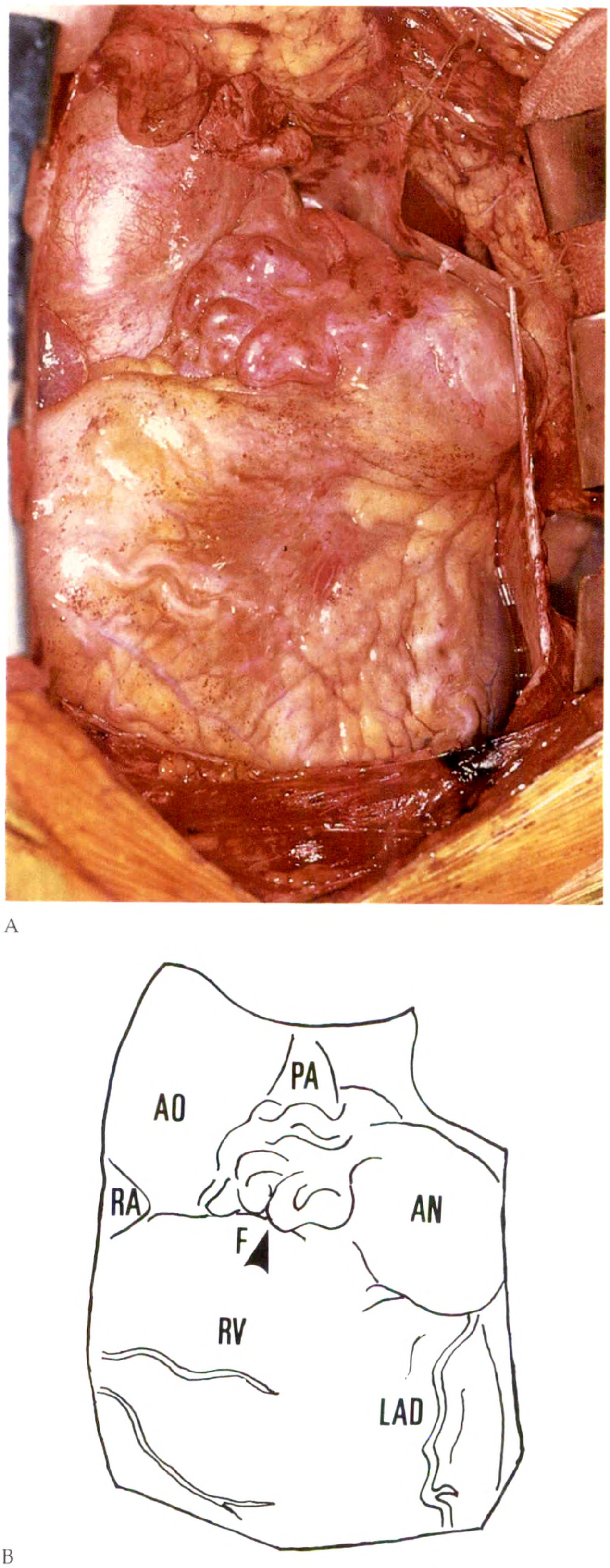


Fig 3. Operative view. A large tumor 5 cm in diameter was located between the right ventricular outflow tract and left anterior descending coronary artery (LAD). *Several tortuous vessels were observed anterior to the main pulmonary artery* (PA). (AN = *aneurysm of coronary fistula;* AO = *ascending aorta;* F and arrowhead = *coronary fistula;* RA = *right atrium;* RV = *right ventricle.)*

surgical correction of coronary arteriovenous fistula connecting to the main pulmonary artery in a patient presumed to have patent ductus arteriosus. They stated that the fistula was aneurysmal. Although spontaneous rupture of a coronary fistula is very rare [6, 9], despite the fact that the feeding coronary artery or the fistula itself may become aneurysmal, progressive dilatation of the coronary fistulous aneurysm, as with other aneurysms, mandates early resection of the aneurysm and closure of the fistula.

References

1. Hobbs RE, Millit HD, Raghavan PV, Moodie DS, Sheldon WC. Coronary artery fistulae: a 10-year review. Cleve Clin Q 1982;49:191–7.
2. Liberthson RR, Sagar K, Berkoben JP, Weintraub RM, Levine FH. Congenital coronary arteriovenous fistula: report of 13 patients, review of the literature and delineation of management. Circulation 1979;59:849–54.
3. Neufeld HN, Lester RG, Adams P Jr, Anderson RC, Lillehei CW, Edwards JE. Congenital communication of a coronary artery with a cardiac chamber or the pulmonary trunk ("coronary artery fistula"). Circulation 1961;24:171–9.
4. Swaye PS, Fisher LD, Litwin P, et al. Aneurysmal coronary artery disease. Circulation 1983;67:134–8.
5. Robinson FC. Aneurysms of the coronary arteries. Am Heart J 1985;109:129–35.
6. Edwards JE. Anomalous coronary arteries with special reference to arteriovenous-like communications. Circulation 1958; 17:1001–6.
7. Urrutia CO, Falaschi G, Ott DA, Cooley DA. Surgical management of 56 patients with congenital coronary artery fistulas. Ann Thorac Surg 1983;35:300–7.
8. Bjork G, Crafoord C. Arteriovenous aneurysm on the pulmonary artery simulating patent ductus arteriosus botalli. Thorax 1947;2:65–8.
9. Habermann JH, Howard ML, Johnson ES. Rupture of the coronary sinus with hemopericardium. Circulation 1963;28: 1143–4.

Bilateral Elastofibroma Dorsi

Hans-Günther Machens, MD, Ruth Mechtersheimer, MD, Ulrich Göhring, MD, and Peter N. Schlag, MD, PhD

Department of Surgery and Institute of Pathology, University of Heidelberg, Heidelberg, Germany

Elastofibroma dorsi was diagnosed in a 76-year-old woman with bilateral subscapular tumor masses and a 3-year history of recurrent, right-sided scapular pain. A bilateral tumor extirpation was performed and the patient left the hospital free of symptoms 10 days later. We suggest that both constant trauma with resulting excessive elastin production and collagen degeneration might play a major role in the pathogenesis of this rare proliferative lesion.

(Ann Thorac Surg 1992;54:774–6)

Elastofibroma is a rare, benign connective tissue proliferation first described 1961 by Jarvi and Saxen [1] in a series of 4 patients. It is commonly found in the subscapular region beneath the rhomboid and latissimus dorsi muscles, hence the name "elastofibroma dorsi." The pathogenesis of this lesion has been controversial. Two main theories have been proposed, suggesting either true neoplasia or reactive tissue proliferation. This article describes an additional case of bilateral elastofibroma dorsi with a typical histological and a particular clinical appearance.

A 76-year-old woman was admitted to our inpatient clinic with bilateral, painful soft-tissue masses located in the subscapular region. She had a 3-year history of recurrent, right-sided subscapular pain mainly occurring during housework. The pain became more and more constant and motion-independent with bilateral intercostal radiation. Six weeks before admission she palpated for the first time a right-sided subscapular tumor while taking a shower. Physical examination revealed bilateral soft-tissue tumors only visible and palpable distal to the inferior angle of the scapula during flexion of the pectoral girdle. When she returned into a neutral position, the masses "flipped back" below the inferior scapular margins (Fig 1). The tumors measured about 12 × 5 cm on the right side and 7 × 5 cm on the left side. Preoperative chest magnetic resonance imaging showed bilateral solid, unencapsuled masses with a heterogenous composition of fibrous and adipose tissues (Fig 2). Chest roentgenogram was normal, and laboratory data were without any pathological findings.

Bilateral tumor extirpation was performed. On both sides a dense, fibroelastic mass protruded after dissection of the latissimus dorsi muscles. Although both lesions were ill-defined and had no capsule, muscular infiltration was not found. However, the tumors adhered to the scapular periosteum for a length of 2 cm. The left-sided tumor invaded the periosteum of the sixth and seventh ribs. Both tumors were removed in toto, including the adherent periosteum. The tumors measured 12 × 5 × 3 cm on the right side and 7 × 5 × 3 cm on the left side.

On cut surface both lesions were ill-defined, firm, and

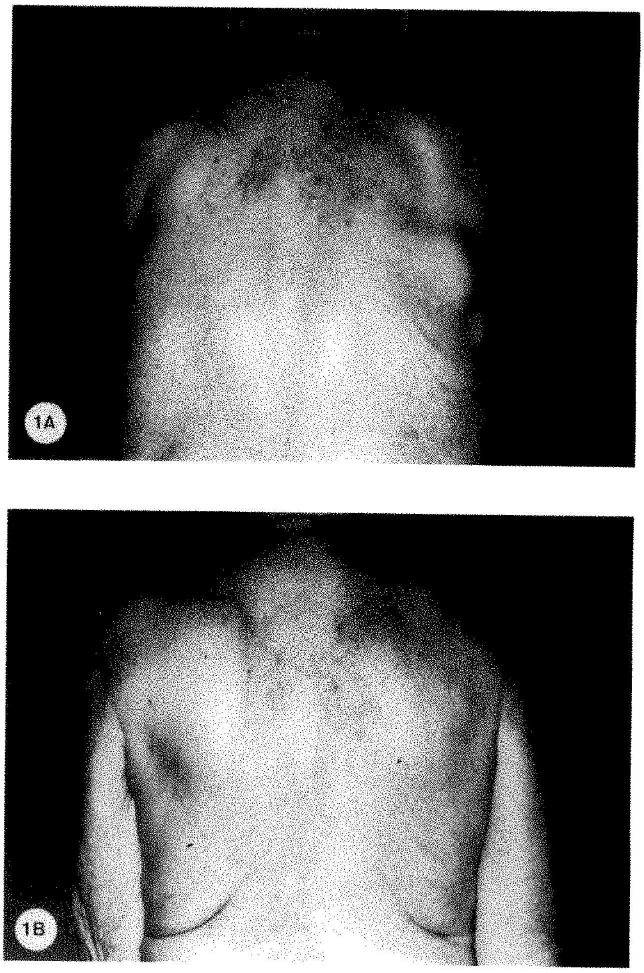


Fig 1. Bilateral subscapular elastofibroma. The tumors protruded from beneath the scapulae by flexion of the shoulder girdle (A). When the patient returned to the neutral position, the masses flipped back below the inferior scapular margins (B).

Accepted for publication Jan 15, 1992.

Address reprint requests to Dr Machens, Department of Abdominal and Transplantation Surgery, Medical School Hannover (MHH), Konstanty-Gutschow Str 8, 3000 Hannover 61, Germany.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

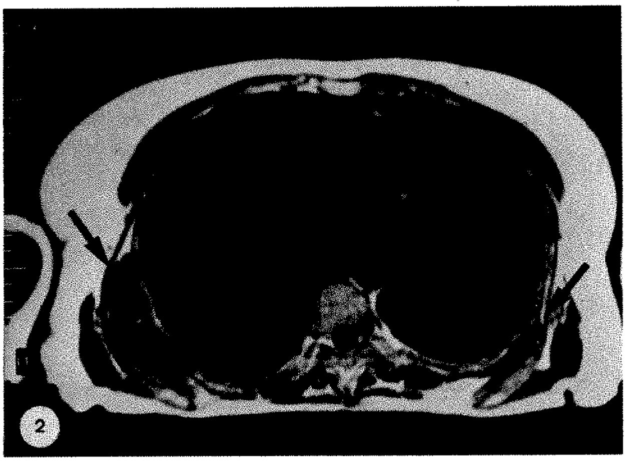


Fig 2. Chest magnetic resonance image showing bilateral solid, unencapsuled masses with a heterogenous composition of fibrous and adipose tissues.

whitish-yellow. Histologically, both tumors exhibited an identical picture of jointly intertwining collagen and elastic fibers with many intermingled small blood vessels (Fig 3a). Most of the elastic fibers were fragmented into small leaflike globules (Fig 3b), between which occasional fibroblasts were identified. Islands of mature adipose tissue varying in size were found within the proliferations. Additionally, small amounts of degenerative mucoid material were found in the bigger, right-sided tumor.

Comment

Since its first description by Jarvi and Saxen [1] more than 170 cases of elastofibroma dorsi have been documented in the literature [2]. Elastofibromas do not exclusively occur in the infrascapular and subscapular area. Uncommon locations have been reported including deltoid muscle; ischial tuberosity; greater trochanter; olecranon; thoracic wall; foot; stomach; intraspinal, orbital, and inguinal areas [3]; and even tricuspid valve [4]. The vast majority of elastofibromas dorsi are found in the elderly population, with a female-to-male ratio of 8:1 [3]. The tumor incidence may be higher than presumed because several cases of subclinical, occult elastofibroma have been reported [5].

Growth rates of these tumors are not known due to their location and common subclinical behavior. Nagamine and associates [2] reported a range from 1 day to 67 years between onset of symptoms and treatment in their clinicopathological study of 170 cases. Marin and coworkers [6] followed up a patient over a period of 8 years "with only a modest increase in size with respect to total body growth." The histological appearance of elastofibroma clearly defines this tumor as a benign proliferation without malignant changes. Some authors have proposed the term *pseudotumor* for this lesion [7, 8]. Tumor recurrence after excision has been reported only once [2] in the literature.

Indeed, the pathogenesis of elastofibromas has been discussed controversely. Because this tumor is often found in locations exposed to mechanical stress [2–4], an association of heavy manual labor, mechanical stress, and tumor growth has been assumed, especially in lesions occurring bilaterally. Jarvi and associates originally considered the lesion to be caused by "friction of the scapular apex against the ripped thorax," [1] and later described "marked hypertrophy of the elastic constituents followed by degeneration" [7] as a possible pathogenetic factor. The role of fibroblasts producing excessive amounts of elastic matrix as a result of constant trauma has been emphasized by several authors [9, 10]. On the other hand, Stemmerman and Stout [11] suggested elastotic degeneration of collagen fibers as a major pathogenic factor. These authors, as well as Marin and co-workers [6], found no correlation between muscular effort and tumor growth in their cases. Additionally, Nagamine and associates [2] reported several cases of multiple familial occurrence in their study of 170 cases, suggesting a possible genetic factor.

Histologically, our patient had multiple small blood vessels intermingling between fibrous and collagenous

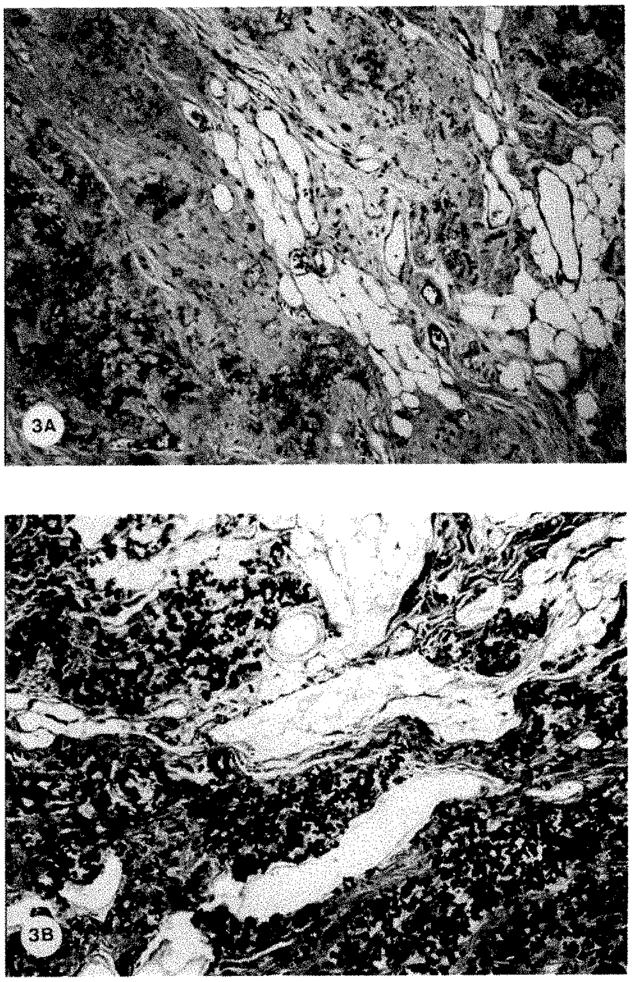


Fig 3. (A) Histologically, the tumors consisted of a mixture of swollen collagen and elastic fibers associated with occasional fibroblasts and small aggregates of mature fat cells. (B) Elastica-van Gieson stain revealed characteristic leaflike globules of the elastic fibers. (Both ×90 before 32% reduction.)

streaks in both tumors. Also, mucoid degeneration was apparent histologically in the bigger, right-sided tumor. We believe that constant trauma with resulting excessive elastin production and collagen degeneration might play a major role in the pathogenesis of this tumor. A diagnosis of elastofibroma must be considered in elderly patients, especially women, who have unilateral or even bilateral subscapular or infrascapular masses. Chest roentgenogram may be normal. Nuclear magnetic resonance and computed tomography are helpful tools to delineate the tumorous masses from thoracic wall and scapula. Each tumor should be evaluated histologically to differentiate this lesion from fibromatosis and other kinds of proliferative, semimalignant or even malignant neoplasias.

Complete surgical excision is the treatment of choice in patients with clinical symptoms. If patients are free of symptoms, an incisional biopsy is mandatory to rule out malignancy. If the tumor is irresectable due to local expansion, in cases of local recurrence [2], or in patients with high medical-anesthetic risk, radiotherapy has been described as a helpful therapeutic option [12].

References

1. Jarvi OH, Saxen E. Elastofibroma dorsi. Acta Pathol Microbiol Scand 1961;144:83–4.
2. Nagamine N, Nohara Y, Ito E. Elastofibroma in Okinawa: a clinicopathologic study of 170 cases. Cancer 1982;50:1794–805.
3. Bennett KG, Organ CH, Cook S, Pitha J. Bilateral elastofibroma dorsi. A case report. Surgery 1988;103:605–7.
4. Mohan C, Goel PK, Gambhir DS, et al. Calcified mobile papillary fibroelastoma of the tricuspid valve: a case report. Ind Heart J 1987;39:237–9.
5. Jarvi OH, Oansimies PH. Subclinical elastofibromas in the scapular region in an autopsy series. Acta Pathol Microbiol Scand 1975;83:87–108.
6. Marin ML, Perzin KH, Markowitz AM. Elastofibroma dorsi: benign chest wall tumor. J Thorac Cardiovasc Surg 1989;98:234–8.
7. Jarvi OH, Saxen AE, Hopsu-Have VK, et al. Elastfibroma—a degenerative pseudotumor. Cancer 1969;23:42–63.
8. Ramos CV, Gillespie W, Narconis RJ. Elastofibroma: a pseudotumor of myofibroblasts. Arch Pathol Lab Med 1978;102:538–40.
9. Winkelmann RK, Sams W Jr. Elastofibroma: report of a case with special histochemical and electron-microscopic studies. Cancer 1969;23:406–15.
10. Dixon AY, Lee SH. An ultrastructural study of elastofibromas. Hum Pathol 1980;11:257–62.
11. Stemmerman GN, Stout AP. Elastofibroma dorsi. Am J Clin Pathol 1962;27:499–506.
12. Deutsch GP. Elastofibroma dorsalis treated with radiotherapy. Br J Radiol 1974;47:621–3.

Double-Lung Transplantation Using Donor Lungs With a Right Tracheal Bronchus

Pierre Y. Brichon, MD, Dominique Blin, MD, Ignacio Perez, MD, Christophe Pison, MD,
François Blanc-Jouvan, MD, Isabelle Pin, MD, Didier Barnoud, MD,
Elisabeth Brambilla, MD, and René Latreille, MD

Department of Thoracic Surgery, Hopital A. Michallon, La Tronche, France

A 58-year-old man underwent sequential bilateral lung transplantation. On the donor heart-lung block, it was discovered that the right apical segment was supplied by a tracheal bronchus. After the separate implantation of both lungs, a right apical segmentectomy was performed and the postoperative course was uneventful. The management of this problem is discussed.

(Ann Thorac Surg 1992;54:777–8)

Lung transplantation has been established as an effective modality for the treatment of select patients with pulmonary disease. We report a case of sequential double-lung transplantation in which the right apical segment of the donor lungs was supplied by a tracheal bronchus arising from the trachea.

The patient is a 58-year-old man with respiratory insufficiency related to an obliterative bronchiolitis. This pulmonary disease was related to D-penicillamine treatment instituted because of a rheumatoid disease. Some chronic bronchial infection was present in both lungs, and we decided to perform a sequential double-lung transplantation.

On April 16, 1991, a 35-year-old man was considered a suitable lung donor. He had no particular thoracic history, a good chest roentgenogram, and a good blood gas analysis. No fiberoptic bronchoscopy was performed. En bloc harvesting of the heart and lungs was performed. The lungs were preserved with an infusion of prostacyclin in the pulmonary artery, followed by blood pneumoplegia as recommended by the Papworth group [6]. Hartman cardioplegia was used. The heart was excised from the heart-lung block and successfully implanted by a surgical cardiac unit 200 km distant. The two-lung block was then stored in a cold saline fluid, inside an iced bag.

The recipient's chest was entered using a double thoracotomy approach with transverse sternal splitting. Cardiopulmonary bypass was instituted between the aortic root and the right atrium without cardiac arrest and using normothermia (33°C).

When the two donor lungs were prepared for implantation, it was observed that the right apical segment was supplied by a tracheal bronchus arising from the right side of the trachea, 1 cm above the right main bronchus (Fig 1). It was decided to deal with this problem by a right apical segmentectomy. Each lung was separately implanted using three anastomoses in each hilum: (1) bronchial anastomosis as distal as possible, with absorbable running suture, (2) venous anastomosis, and (3) arterial anastomosis. The ischemic time for right and left lungs was, respectively, 2 and 3 hours. Both lungs were inflated and reperfused and then the apical segmentectomy was performed; after ligation of the apical artery, the right intersegmental plan was reconstituted by gentle traction on the apical bronchus. To avoid postoperative air leak, the raw edges were sutured together with an absorbable running suture.

After the patient was weaned from cardiopulmonary bypass, each bronchial anastomosis was encircled by a pericardial pedicled flap. Two chest tubes were placed inside each pleural cavity. The postoperative course was uneventful. The patient was extubated on the second postoperative day and reintubated from the third to the seventh postoperative days because of a respiratory muscle weakness. A right air leak was observed on the first postoperative day only, and the chest tubes were removed from both sides on the seventh and eighth postoperative days without any postoperative pneumothorax.

The chest roentgenogram showed an apical pleural thickening at the top of the right side of the chest and few parenchymal sequelae of segmentectomy. The patient was discharged from the intensive care unit on the 13th postoperative day with a routine immunosuppressive regimen. He left the chest medical unit on the 35th postoperative day with good pulmonary performance and no longer on oxygen support. Neither rejection nor serious infection occurred. He is alive and well 6 months after the transplantation.

Comment

Among the three possible techniques of lung transplantation (eg, heart-lung, double-lung, and single-lung transplantation), the double-lung technique is evolving from an "en block" fashion with a tracheal anastomosis to a sequential double-lung technique with two bronchial anastomoses [1–3]. These double bronchial anastomoses are now preferred because they carry less risk of dehiscence on the airway suture line than in the case of a tracheal anastomosis [4]. In our patient, lung transplan-

---

Accepted for publication Jan 15, 1992.

Address reprint requests to Dr Brichon, Department of Thoracic Surgery, Hopital A. Michallon, 38700 La Tronche, France.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

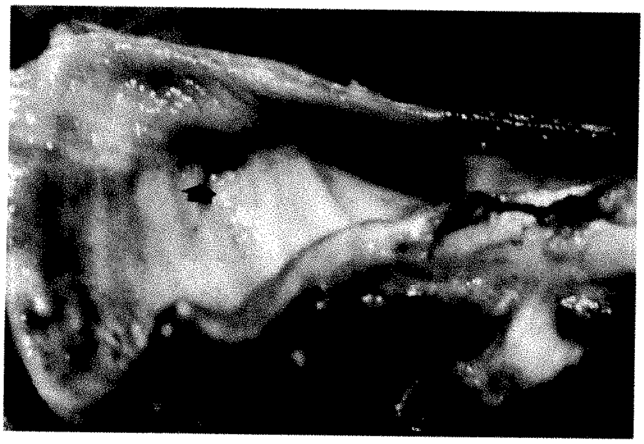


Fig 1. Resected specimen of the donor carina: the tracheal bronchus arises 1 cm above the right main bronchus (arrow).

tation was performed using a right lung with a tracheal bronchus. How should one deal with this problem?

When a right bronchial anastomosis is performed, as in single or double sequential lung transplantation, reimplantation of the tracheal bronchus into the trachea does not seem to be a safe procedure because of the small lumen of the bronchus and the risk of dehiscence or stenosis related to bronchial ischemia [1]. It is necessary to perform, as we did, a segmentectomy of the part of the parenchyma supplied by the abnormal bronchus.

In case of heart-lung transplantation, a tracheal anastomosis is performed and is at low risk of complication because of the carinal vascular supply from the coronary arteries [5]. This anastomosis should be done as distal as possible on the donor trachea to avoid ischemic complications on the suture line [6]. If this ostium of the tracheal bronchus is above the anastomotic site, the best way seems to be not to reimplant it, and to perform a subsequent segmentectomy. If the ostium is under the suture line, it seems better to leave the tracheal bronchus rather than resect it, which would carry a subsequent risk of tracheal leakage and fistula.

We conclude that lung transplantation is feasible even when a tracheal bronchus is present on the right donor lung and that a segmentectomy can be performed during a lung transplant procedure without any risk.

References

1. Noirclerc MJ, Metras D, Vaillant A, et al. Bilateral bronchial anastomosis in double lung and heart-lung transplantations. Eur J Cardiothorac Surg 1990;4:314–7.
2. Patterson GA, Maurer JR, Williams TJ, Cardoso PG, Scavuzzo M, Todd TR. Comparison of outcomes of double and single lung transplantation for obstructive lung disease. J Thorac Cardiovasc Surg 1991;101:623–32.
3. Kaiser LR, Pasque MK, Trulock EP, Low DE, Dresler CM, Cooper JD. Bilateral sequential lung transplantation: the procedure of choice for double-lung replacement. Ann Thorac Surg 1991;52:438–46.
4. Patterson GA, Todd TR, Cooper JD, Pearson FG, Winton TL, Maurer J. Airway complications after double lung transplantation. J Thorac Cardiovasc Surg 1990;99:14–21.
5. Gensini GG, Bruto da Costa BC. The coronary collateral circulation in living man. Am J Cardiol 1969;24:393–400.
6. Jamieson SW, Kaye MP. Operative procedure and postoperative management. In: Wallwork J, ed. Heart and heart-lung transplantation. 1st ed. Philadelphia: W.B. Saunders, 1989:481.

Surgical Management of Left Coronary Artery Ostial Atresia and Supravalvar Aortic Stenosis

Eliot R. Rosenkranz, MD, Daniel J. Murphy, Jr, MD, and Delos M. Cosgrove III, MD

Departments of Thoracic and Cardiovascular Surgery and Pediatric Cardiology, The Cleveland Clinic Foundation, Cleveland, Ohio

Congenital atresia of the left main coronary artery ostium is a rare lesion, particularly when found in association with supravalvar aortic stenosis. This report describes the preoperative evaluation and surgical management of this lesion found in conjunction with a quadricuspid aortic valve in a 5-year-old child. Patch aortoplasty and left internal thoracic artery to left anterior descending coronary artery bypass were performed to correct this lesion.

(Ann Thorac Surg 1992;54:779–81)

An association between supravalvar aortic stenosis and left coronary artery ostial stenosis is well recognized, particularly in the setting of Williams syndrome [1]. True atresia of the left coronary ostium and left main coronary artery as isolated lesions are quite rare, with fewer than 30 reported cases in the world literature. Left coronary ostial atresia with supravalvar aortic stenosis is even more infrequent, with only 5 reported cases to date. This report describes the surgical management of a child with symptoms of myocardial ischemia due to supravalvar aortic stenosis and atresia of the left coronary artery ostium in whom a competent quadricuspid aortic valve was also found.

A 5-year-old girl had a 2-year history of episodes of pallor, nausea, and emesis after moderate exertion. On examination she was acyanotic with normal facies. Her cardiac examination revealed a thrill in the suprasternal notch and a grade 3/6 systolic ejection murmur at the left sternal border with radiation to the neck.

The electrocardiogram revealed left axis deviation and left ventricular hypertrophy. A two-dimensional Doppler echocardiographic study revealed supravalvar aortic stenosis with an estimated gradient of 50 mm Hg. Left ventricular size and function were normal although severe concentric left ventricular hypertrophy was present.

Left heart catheterization and angiography confirmed the presence of a supravalvar aortic gradient. Although an aortic root contrast injection showed a large right coronary artery with delayed filling of the left coronary system, atresia of the left coronary artery ostium was not initially recognized.

At operation to relieve the supravalvar aortic stenosis, a thick ridge was noted at the sinotubular junction. Excision allowed inspection of the aortic valve, which was quadricuspid with a dominant right coronary cusp and a small, but not hypoplastic left coronary cusp. The right coronary artery ostium was large in size and normal in position. The left coronary ostium was atretic with only a small dimple present in the left sinus of Valsalva. The supravalvar narrowing was relieved with a Gore-Tex patch (W. L. Gore & Assoc, Naperville, IL). No residual supravalvar obstruction or aortic insufficiency was noted on the postoperative echocardiogram. Left ventricular function was normal, and the electrocardiogram revealed transient ST segment elevation in the anterior precordial leads.

The child remained asymptomatic until 15 months later, when an exercise treadmill test induced angina with severe ST segment depression in the anterior precordial leads at low work levels. A selective coronary angiogram confirmed atresia of the left coronary artery ostium (Fig 1). Due to symptoms and signs of myocardial ischemia, she was reoperated on to establish antegrade perfusion of the left coronary artery bed.

After secondary sternotomy, a 1.5-mm-diameter left internal thoracic artery was anastomosed to the proximal left anterior descending coronary artery using interrupted 7-0 silk suture. There was no evidence of myocardial injury on the postoperative electrocardiograms. A repeat angiogram before discharge confirmed the patency of the left internal thoracic artery–left anterior descending coronary artery graft (Fig 2). She remains asymptomatic with normal exercise tolerance.

Comment

Anomalies of coronary artery origin and distribution represent less than 1% of all congenital heart lesions [2]. In infancy, anomalous origin of the left coronary artery from the pulmonary artery is the most common cause of symptomatic myocardial ischemia and heart failure. Stenotic coronary artery lesions in infancy and early childhood are most frequently due to inflammatory conditions such as Kawasaki disease. Most types of anomalous origins of the coronary artery ostia from the aorta are

---

Accepted for publication Jan 16, 1992.

Address reprint requests to Dr Rosenkranz, Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195-5066.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

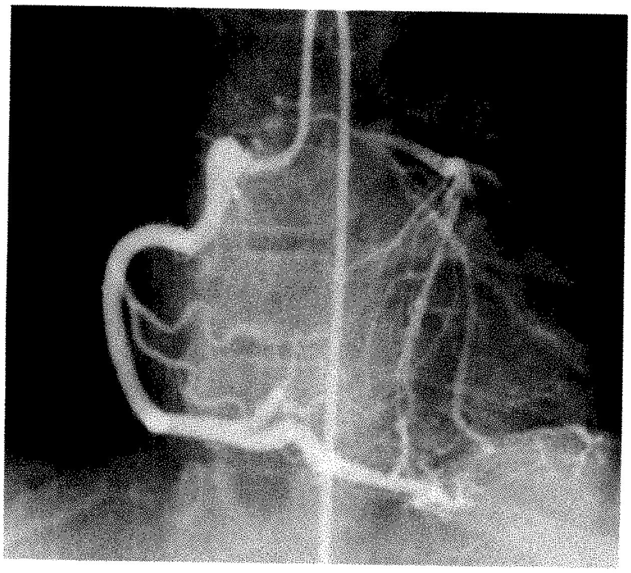


Fig 1. Selective contrast injection of right coronary artery. Note retrograde filling of left coronary system by collaterals and atresia of the majority of the left main coronary artery.

silent symptomatically. Although atresia of the left coronary ostium is often considered a single coronary artery system, these lesions differ anatomically and pathophysiologically. In single coronary artery anatomy, blood flow in the right and left coronary beds is antegrade through the continuous, solitary coronary artery. With atresia of the left coronary artery ostium, left coronary artery perfusion is supplied retrograde through collaterals. This may be inadequate during exercise, resulting in symptoms of ischemia including sudden death. Supravalvar aortic stenosis with coronary ostial atresia increases the likelihood of exercise-induced ischemia due to the added myocardial oxygen requirement imposed by the pressure-loaded, hypertrophied left ventricle. The onset of symptoms may coincide with progression of the supravalvar gradient or be due to inadequate collateral supply to meet the oxygen demands of exercise. The resolution of symptoms in our patient after the relief of the supravalvar obstruction supports these mechanisms.

The diagnosis of atresia of the left coronary ostium may be suspected when a prominent right coronary artery system and late opacification of the left coronary artery system are seen on aortic root contrast injection. Selective ostial injection provides more precise confirmation of the anatomy, demonstrating the inability to opacify the left coronary system by antegrade injection. Coronary revascularization with saphenous vein or internal thoracic artery grafts in children has most frequently been used for the treatment of segmental stenoses associated with Kawasaki disease. We are aware of 4 additional cases where the left internal thoracic artery was used to treat symptomatic myocardial ischemia associated with atresia of the left main coronary ostium [3–6].

This case was unusual because of the coexistence of a quadricuspid aortic valve in conjunction with atresia of the left coronary ostium and supravalvar aortic stenosis. Several authors have reported anomalous aortic valve leaflets in tricuspid and quadricuspid aortic valves obstructing the left coronary artery ostium, which may be seen clinically in a manner similar to our patient [7, 8]. Because septation of the embryonic arterial trunk and development of the aortic valve leaflets occur temporally just after development of the coronary artery origins from the sinuses of Valsalva, one can speculate that a single developmental error might result in this constellation of anomalies of the aortic root.

This case reemphasizes the need to consider coronary artery obstructions or atresia in children with symptoms of myocardial ischemia. Selective coronary angiography is required to fully define the pathologic anatomy such that surgical revascularization may accompany repairs of additional cardiac lesions.

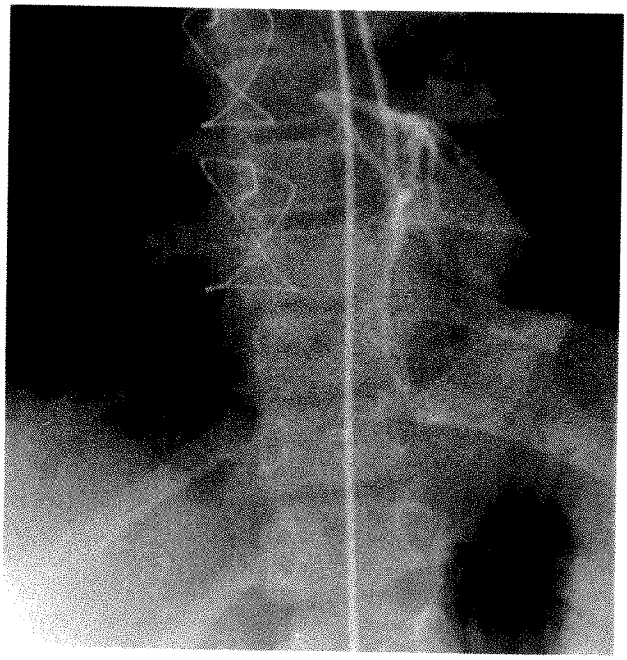


Fig 2. Postoperative injection of left internal thoracic to left anterior descending coronary artery bypass graft.

References

1. Cornell WP, Elkins RC, Criley MJ, Sabiston DC. Supravalvular aorta stenosis. J Thorac Cardiovasc Surg 1966;51:484–92.
2. Byrum CJ, Blackman MS, Schneider B, Sondheimer HM, Kavey REW. Congenital atresia of the left coronary ostium and hypoplasia of the left main coronary artery. Am Heart J 1980;99:354–8.
3. Fortune RL, Baron PJ, Fitzgerald JW. Atresia of the left main coronary artery: repair with left internal mammary artery bypass. J Thorac Cardiovasc Surg 1987;94:150–1.
4. Leitz KH, Oster H, Kentel J. Use of the left internal thoracic artery to correct a left main coronary atresia. Thorac Cardiovasc Surg 1987;35:345–7.

5. Koh E, Nakagawa M, Hamaoka K, Sawaka T, Oga K. Congenital atresia of the left coronary ostium: diagnosis and surgical treatment. Pediatr Cardiol 1989;10:159–62.
6. Sato S, Majima T, Kawaguchi T, Kitagawa S, Takano H, Ihara K. Congenital atresia of the left main coronary artery ostium. A case suffering from ventricular tachycardia. J Jpn Assoc Thorac Surg 1990;38:1467–74.
7. Waxman MB, Kong Y, Behar VS, Sabiston DC, Morris JJ. Fusion of the left aortic cusp to the aortic wall with occlusion of the left coronary ostium and aortic stenosis and insufficiency. Circulation 1970;41:848–57.
8. Kurosawa H, Wagenaar SS, Becker AE. Sudden death in a youth. A case of quadricuspid aortic valve with isolation of the origin of the left coronary artery. Br Heart J 1981;46:211–5.

REVIEW OF RECENT BOOKS

Mediastinal Surgery
Edited by Thomas W. Shields, MD
Philadelphia, Lea & Febiger, 1991
400 pp, illustrated, $85.00

Reviewed by James L. Nielsen, MD

This work very effectively serves an area of thoracic surgery that is usually under-represented in most texts. In it, the editor organizes and unifies contributions from 35 different authors, including himself. Throughout, he also applies a unique organization of the mediastinum, dividing it into anterior and visceral segments instead of the usual four compartments. This approach works very well in this text.

The book begins with a thorough section on the anatomy of the mediastinum and then moves on to diagnostic investigations, including in-depth descriptions of invasive diagnostic procedures such as standard cervical mediastinal exploration, extended cervical mediastinal exploration, and substernal cervical mediastinal exploration. A short section on mediastinal infections and their management is included.

The section on the overview of mediastinal mass lesions gives the reader the "big picture" on this topic, with individual causes being discussed in the subsequent sections. Thymoma, lymphomas, germ cell tumors, neuroendocrine tumors, and mediastinal cysts are covered. In each section, comprehensive information about diagnosis, prognosis, and therapy, both surgical and nonsurgical, is presented. Also given equal attention are syndromes associated with mediastinal lesions, such as myasthenia gravis and superior vena caval syndrome.

The text finishes with a section on less common procedures, such as various approaches to thymectomy, management of hourglass tumors of the paravertebral sulcus, and thoracic duct ligation, all of which are well-described and illustrated.

One of the few complaints that readers may have with this book is that the descriptions of various diseases, especially of the thymus, are separate from the discussion of the surgical approach to the problem. This is lessened by the adequate references to relevant information in other chapters.

Overall, this book is easily read due to the concise writing style. Also, it is well-illustrated with clear drawings and high-quality reproductions of chest radiographs, computed tomograms, and magnetic resonance images. It is as excellent a resource for thoracic surgeons-in-training or as a refresher for surgeons in practice when confronted with some of these less common clinical problems.

San Antonio, Texas

Hyperbaric Oxygen: Value in Management of Nonhealing Saphenectomy Wounds

Michael D. Horowitz, MD, Carmen G. Portogues, PA, Luis A. Matos, MD, and Robert W. McGowan III, PA

Division of Thoracic and Cardiovascular Surgery and Division of Hyperbaric Medicine, University of Miami/Jackson Memorial Medical Center, Miami, Florida

The greater saphenous vein is commonly used as a conduit for arterial bypass in both cardiac and peripheral vascular operations. Although saphenectomy wound complications occur infrequently, such problems may be quite serious. We report a case in which hyperbaric oxygen therapy was extremely valuable in the management of a very difficult saphenectomy wound.

(Ann Thorac Surg 1992;54:782–3)

The greater saphenous vein is commonly used as a bypass conduit for operations involving the coronary and peripheral arterial circulation. Major complications related to the saphenectomy wound occur in a small minority of patients. Nevertheless, such problems may be a cause of serious and prolonged morbidity. The purpose of this article is to present a case in which hyperbaric oxygen (HBO) therapy proved very valuable in the management of a difficult saphenectomy wound.

A 61-year-old woman underwent a triple coronary artery bypass using the left internal mammary artery and the left greater saphenous vein. She had diabetes mellitus, which was treated with oral hypoglycemic medication. She did not smoke tobacco. The left dorsal pedal pulse was normal to palpation; the posterior tibial pulse was not palpable, but flow was readily detected using a Doppler probe. Recovery from operation was uncomplicated, and the saphenectomy site appeared to be healing appropriately when the patient was discharged home 10 days postoperatively.

On the thirteenth postoperative day, breakdown of the saphenectomy wound developed with ischemic changes of the skin edges. Initial management consisted of debridement, dressings, and systemic antibiotics. Despite these measures, there was progressive ischemic necrosis of the wound edges and base. Severe hypoxia of the tissues adjacent to the wound, with an oxygen tension of less than 5 mm Hg, was demonstrated by transcutaneous measurement. There was no improvement in local tissue oxygenation with an inspired oxygen concentration of approximately 100%.

Hyperbaric oxygen therapy was instituted with two 90-minute sessions per day to 2.4 atmospheres absolute with 100% O_2. The tissue oxygen tension measured during treatment was approximately 450 mm Hg. The wound improved rapidly, and skin graft coverage was accomplished 2 weeks after initiation of HBO therapy. Fifteen additional HBO treatments were administered over the next 2 weeks. Examination in the clinic 5 weeks after completion of HBO therapy showed the wound to be healing well (Fig 1). There have been no wound problems during 13 months of follow-up.

Comment

The greater saphenous vein is an extremely useful arterial bypass graft. Many of the patients who have the saphenous vein used for this purpose are afflicted with peripheral vascular insufficiency, diabetes mellitus, or both. Nevertheless, serious saphenectomy wound complications are encountered infrequently.

Wound healing requires an oxygen tension of 30 to 40 mm Hg. With HBO, a tissue oxygen tension as high as 1,500 mm Hg can be achieved. The therapeutic effect of HBO is a result of several factors [1]. First, there is a substantial increase in the amount of oxygen available for cellular metabolism. Second, the function of leukocytes is enhanced when the tissue oxygen tension is raised above

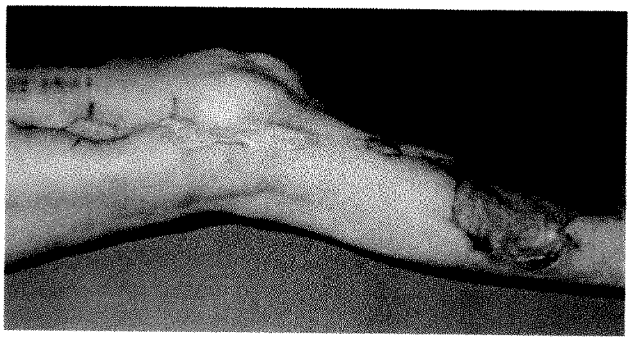


Fig 1. The extent of breakdown of the saphenectomy wound is seen. The wound is well healed 7 weeks after skin grafting and 5 weeks after completion of hyperbaric oxygen therapy.

Accepted for publication Jan 24, 1992.

Address reprint requests to Dr Horowitz, Division of Thoracic and Cardiovascular Surgery, University of Miami School of Medicine, PO Box 016960 (R-114), Miami, FL 33101.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

30 mm Hg. Also, HBO promotes fibroblast activity and collagen synthesis, which support angioneogenesis in hypoxic tissues [2].

Hyperbaric oxygen has been shown to be useful in the management of various complex wound problems [1, 2]. Furthermore, HBO has been shown to improve the survival of compromised skin flaps [2].

Hyperbaric oxygen therapy should be considered as a valuable adjunct for management of difficult saphenectomy wounds if appropriate facilities are available locally or the patient's condition warrants transfer to an institution with HBO capability.

References

1. Grim PS, Gottlieb LJ, Boddie A, Batson R. Hyperbaric oxygen therapy. JAMA 1990;263:2216-20.
2. Undersea and Hyperbaric Medical Society. Hyperbaric oxygen therapy: a committee report. Bethesda, MD: Undersea and Hyperbaric Medical Society, 1989.

Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hilton Executive Conference Center, Dallas Fort Worth Airport, Dallas, TX, on February 13, 1994. The closing date for registration is August 1, 1993.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Pericardial Repair of a Tracheal Laceration During Transhiatal Esophagectomy

Lyall A. Gorenstein, MD, James G. Abel, MD, and G. Alexander Patterson, MD

Division of Thoracic Surgery, University of Toronto, Toronto, Ontario, Canada

Transhiatal esophagectomy has recently been popularized for both benign and malignant esophageal disease. While we were performing a transhiatal esophagectomy for a squamous cell cancer of the upper third of the esophagus, a tear in the membranous trachea near the carina occurred. This was repaired through the cervical incision with a free pericardial patch. This solution to a potentially catastrophic complication of transhiatal esophagectomy gave a satisfactory result without early or late postoperative respiratory complications.

(Ann Thorac Surg 1992;54:784–6)

Transhiatal esophagectomy for carcinoma was first performed by Turner [1] in 1913. It was used by Ong and Lee [2] to restore swallowing in patients with carcinomas of the cervical esophagus or pharynx requiring pharyngolaryngectomy. Orringer and Orringer [3] have popularized this procedure for both benign disorders of the esophagus requiring esophagectomy and all resectable malignancies of the esophagus. When the survival results of transhiatal esophagectomy are compared with those of esophagectomy with thoracotomy from the same institution, there is no significant difference [4, 5]. The major advantages of transhiatal esophagectomy are the reduction in pulmonary morbidity associated with a thoracotomy and the relative safety of a cervical esophagogastric anastomosis. Two major criticisms of this procedure are frequently raised. First, the oncologic principal of wide en-bloc resection including regional lymphadenectomy for gastrointestinal malignancies is violated, thereby reducing the accuracy of pathologic staging. Second, there is potential risk of major intraoperative catastrophe from injury to adjacent mediastinal structures during blunt dissection of the esophagus from the mediastinum. Selection of patients appropriate for transhiatal esophagectomy and knowledge of the management of potential complications are important to ensure the safety of the operation.

A 66-year-old man had 3 weeks of progressive dysphagia for solid foods. The barium swallow demonstrated an irregular eccentric narrowing in the cervical esophagus (Fig 1). Esophagoscopy confirmed an exophytic circumferential squamous cell cancer arising 23 cm from the incisors, extending for 5 cm. Flexible bronchoscopy performed simultaneously showed minor extrinsic compression of the distal membranous trachea but no mucosal invasion. The computed tomographic scan of the thorax showed no invasion beyond the esophagus and no hepatic or lymph node metastases (Fig 2).

A transhiatal esophagectomy was performed. After an initial exploratory laparotomy, the cervical esophagus was dissected through a standard left neck incision. The tumor was not invading the membranous trachea, and mobilization of the tumor from the distal trachea was possible. After completion of gastric mobilization, the thoracic

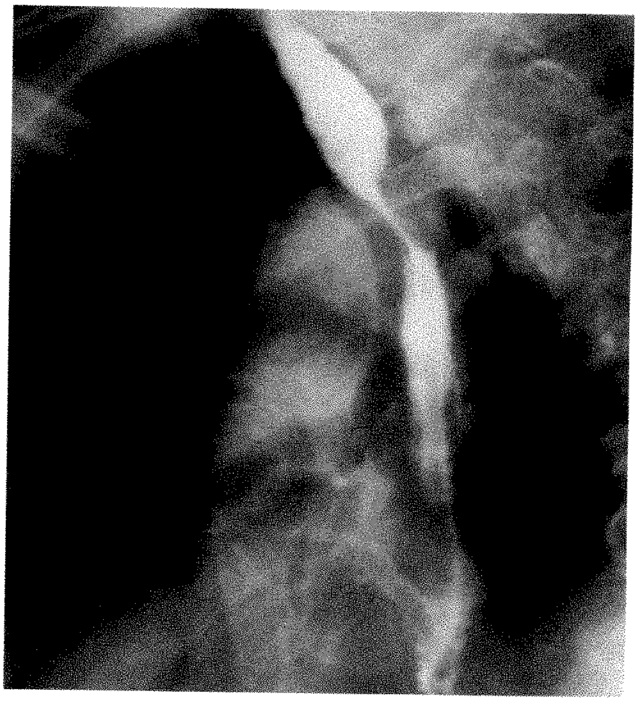


Fig 1. Esophagogram showing a smooth, concentric narrowing approximately 4 cm long in the upper third of the esophagus and a small hiatal hernia. Endoscopy and biopsy confirmed this to be a squamous cell carcinoma.

Accepted for publication Jan 31, 1992.

Presented at the Problem Case Seminar of the Twenty-seventh Annual Meeting of The Society of Thoracic Surgeons, San Francisco, CA, Feb 18–20, 1991.

Address reprint requests to Dr Patterson, Division of Cardiothoracic Surgery, Washington University School of Medicine, 1 Barnes Hospital Plaza, Suite 3108, St. Louis, MO 63110.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

esophagus was dissected through the hiatus. During the transhiatal dissection of the thoracic esophagus, a large air leak developed. Bronchoscopy demonstrated a laceration in the posterior midline of the trachea 3 cm long extending to within 2.5 cm of the carina (Fig 3A). The endotracheal tube was not long enough to be advanced beyond the laceration, so a flexible armored endotracheal tube was placed through the laceration into the left main bronchus (Fig 3B). This stopped the air leak and allowed resumption of ventilation. Esophageal mobilization was completed. A free pericardial flap was harvested through the epigastrium and sutured to the membranous trachea with a continuous Vicryl suture through the cervical incision (Fig 3C). The armored tube was removed intermittently to facilitate suturing of the pericardial patch. The stomach was pulled up through the posterior mediastinum to buttress the repair, and a cervical esophagogastrostomy was performed (Fig 3D). There were no postoperative respiratory complications. Bronchoscopy performed 6

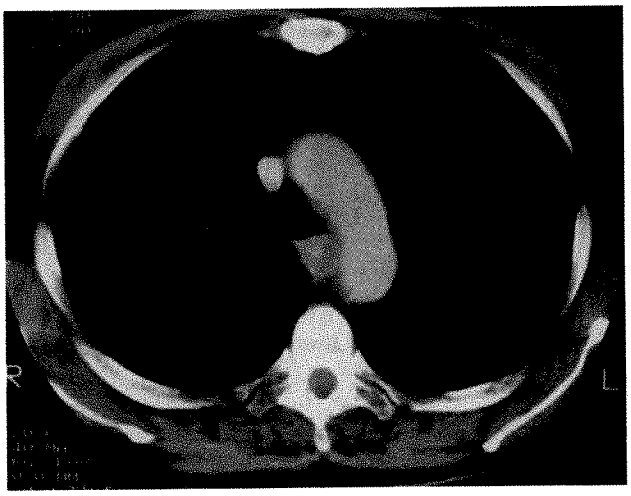


Fig 2. Computed tomogram of the thorax. There is no compression or invasion of the membranous trachea and no mediastinal lymphadenopathy.

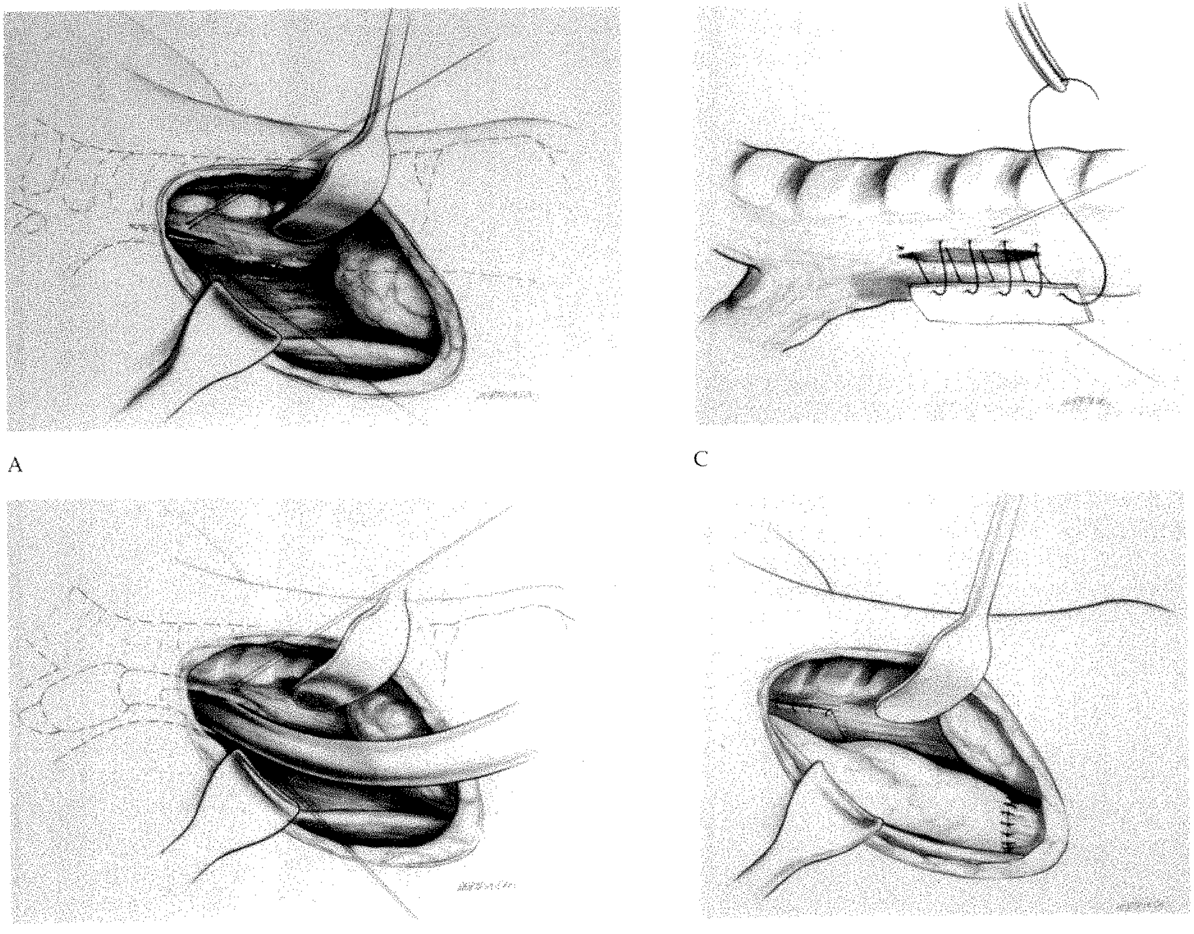


Fig 3. (A) A laceration in the membranous trachea extends to within 2.5 cm of the carina. Only the upper extent is visible through the cervical incision; however, after dissection of the pretracheal fascia, stay sutures improve the exposure. (B) An endotracheal tube is advanced across the operative field through the tracheal laceration into the left main bronchus. (C) A free pericardial patch is sutured to the edge of the membranous trachea. Intermittant apneic intervals are required to perform the repair. (D) After completion of the repair, the gastric tube has been pulled up through the posterior mediastinum and anastomosed to the cervical esophagus.

months later showed complete epithelialization of the pericardial patch.

Comment

Tracheal injury during transhiatal esophagectomy in experienced hands is a relatively infrequent occurrence. The incidence ranges from 0% to 7% [6]. This complication should be preventable. If tumors of the middle third of the esophagus are bulky and long, and tracheal compression is present on computed tomographic scan or bronchoscopy, then mobilization of the thoracic esophagus should be performed under direct vision [7]. However, during transhiatal esophagectomy for benign disease or tumors of the lower third of the esophagus, tracheal injury can occur. Avoiding hyperinflation of the endotracheal tube cuff [8] and deflating it during mediastinal manipulations have been recommended [9]. If there is adherence of the cervical esophagus to the distal trachea an upper sternal split can improve exposure to facilitate the dissection.

Should a tracheal laceration occur, rapid control of the airway is critical. A single-lumen endotracheal tube if left uncut can be advanced into the left main bronchus. Intubation of the distal trachea through the laceration across the operative field may be required if single-lung ventilation is inadequate [10].

Repair of tracheal injuries through the neck incision is preferable, avoiding the additional operative time and morbidity of a thoracotomy. This is facilitated by completing the dissection of the thoracic esophagus after gaining airway control. Opening the pretracheal fascia anteriorly, as when performing mediastinoscopy, helps mobilize the trachea but does not interfere with its blood supply. Traction sutures placed at the junction of the cartilaginous and membranous trachea at the level of the laceration allow cephalad traction to further exposure the defect. Upper sternal split can also improve exposure if the laceration extends to the carina. If adequate exposure to allow precise repair cannot be obtained with these maneuvers, then the stomach should be positioned in the posterior mediastinum and the cervical anastomosis completed. After closure of both incisions a right posterolateral thoracotomy and tracheal repair are performed.

Pericardium is frequently used to repair congenital cardiac anomalies and has been used to replace the membranous trachea [11, 12]. If primary repair of the trachea will narrow the lumen, or be under tension, then a free pericardial patch is an excellent alternative. The pericardium produces an airtight seal to prevent mediastinal contamination. Respiratory epithelium from the edges of the defect eventually covers the pericardium. Placing the gastric tube in the posterior mediastinum buttresses the repair.

References

1. Turner GG. Excision of thoracic esophagus for carcinoma with construction of extrathoracic gullet. Lancet 1933;2:1315–9.
2. Ong JB, Lee TC. Pharyngogastric anastomosis after oesophagopharyngectomy for carcinoma of the hypopharynx and the cervical esophagus. Br J Surg 1960;48:193–6.
3. Orringer MB, Orringer JS. Esophagectomy without thoracotomy: a dangerous operation? J Thorac Cardiovasc Surg 1983;85:72–80.
4. Hankins JR, Attar S, Coughlin TR Jr, et al. Carcinoma of the esophagus: a comparison of the results of transhiatal versus transthoracic resection. Ann Thorac Surg 1989;47:700–5.
5. Goldfaden D, Orringer MB, Appelman HD, Kalish R. Adenocarcinoma of the distal esophagus and gastric cardia. Comparison of the results of transhiatal esophagectomy and thoracoabdominal esophagectomy. J Thorac Cardiovasc Surg 1986;91:242–7.
6. Hankins JR, Miller JE, Attar S, McLaughlin JS. Transhiatal esophagectomy for carcinoma of the esophagus: experience with 26 patients. Ann Thorac Surg 1987;44:123–7.
7. Wong J. Transhiatal oesophagectomy for carcinoma of the thoracic oesophagus. Br J Surg 1986;73:89–90.
8. Smith BAC, Hopkinson RB. Tracheal rupture during anaesthesia. Anaesthesia 1984;39:894–8.
9. Condon HA. Anaesthesia for pharyngolaryngooesophagectomy with pharyngogastrostomy. Br J Anaesth 1971;43:1061–5.
10. Sung HMH, Nelems B. Tracheal tear during laryngopharyngectomy and transhiatal oesophagectomy: a case report. Can J Anaesth 1989;36:333–5.
11. Kron IL, Johnson AM, Morgan RF. Gastrotracheal fistula: a late complication after transhiatal esophagectomy. Ann Thorac Surg 1989;47:767–8.
12. Okike N, Payne WS, Cortese DA, Dines DA. Pericardial reconstruction of the membranous trachea after resection of an adenoid cystic carcinoma. Mayo Clin Proc 1978;53:80.

Limited Vertical Skin Incision for Median Sternotomy

Shoh Tatebe, MD, Shoji Eguchi, MD, Haruo Miyamura, MD, Satoshi Nakazawa, MD,
Hiroshi Watanabe, MD, Masa-aki Sugawara, MD, Jun-ichi Hayashi, MD,
Kazutoshi Date, MD, and Satoru Nakagawa, MD

Department of Thoracic and Cardiovascular Surgery, Niigata University School of Medicine, Niigata City, Japan

The cosmetic deformity of the vertical skin incision for median sternotomy was decreased by using a mechanical traction system to increase exposure at the superior margin of a shorter wound. The limited vertical skin incision did not impede technical surgical maneuvers and produced a scar that was more acceptable than submammary incision or right anterior thoracotomy. The limited skin incision is especially useful in young women with congenital heart disease.

(Ann Thorac Surg 1992;54:787–8)

Median sternotomy is the most common approach to the heart. However, the scar from a vertical skin incision may be unsightly and a source of distress, especially for young women. To avoid this problem, some surgeons have adopted the submammary skin incision [1–3], right anterior thoracotomy, and Y incision. The submammary skin incision and right anterior thoracotomy require that skin flaps be raised to perform a median sternotomy or thoracotomy. This may result in sensory and sympathetic denervation, hypesthesia of the anterior chest wall [2, 3] and decreased sensation and erection of the nipples [3]. Y incision has the advantage of not requiring a tremendous amount of traction, but the disadvantage to be noted is that it causes unsightly granulation at the top of the vertical incision. For this reason, we tried to minimize disfigurement by using a shorter vertical skin incision in young patients.

Technique

A limited vertical skin incision was used in 7 patients (1 boy and 6 girls, age 1 to 18 years) undergoing median sternotomy to correct a congenital heart defect (atrial septal defect in 3 patients and ventricular septal defect in 4). The day before operation, the skin over the sternum was pulled up toward the neck to measure the mobility of the subcutaneous tissue. Under this condition, the point of sternal notch was marked.

On the operating table, the patient was positioned supine, with small pillows under both shoulders to create laxity in the skin of the neck and anterior chest. The skin was scrubbed in the usual manner, and the sternal notch, the point marked on the day before, and the xiphoid process were marked with a sterilized marking pen. The skin incision line was scored using a ruler, and the patient was draped. The skin incision was made from no less than 4 cm below the sternal notch to the xiphoid process and carried down to the sternum, and the periosteum was scored in the midline. The laxity of the subcutaneous tissue was also confirmed by pulling up the top of the incision toward the neck. A limited dissection was performed when the laxity of subcutaneous tissue was not believed to be adequate. The dissection was not carried out over the median edge of the major pectoral muscle. Dissection was needed in only 1 patient, who was an 18-year-old girl with an atrial septal defect.

A pair of U sutures of 1-0 braided silk with small felt pledgets were placed at the top of the incision. These small felt pledgets were used to avoid pressure necrosis of the skin and subcutaneous tissue. The loops of the sutures were connected to a mechanical scapular retractor (Koken Pattern Scapular Retractor; Senko Medical Instruments Manufacturing Co Ltd, Tokyo, Japan) attached to the operating table, and an equal force was applied bilaterally (Fig 1). We did not measure the traction force, but we could feel the intensity of the traction force by palpation of the sutures. The force was adjusted based on the tension on the sutures. The mechanical scapular retractor was the type used widely in thoracic and upper abdominal procedures. The traction exposed the sternal notch, and the median sternotomy was performed in the usual manner using a sternal saw. After aortic cannulation, the traction was reduced slightly to minimize skin trauma.

After the intracardiac repair, the sternum was closed in a standard fashion. A pressure dressing was applied when subcutaneous dissection had been performed.

Adequate cardiac exposure was obtained without difficulty in all patients. The superior border of the skin incision in all patients was inferior to the sternal angle,

---

Accepted for publication May 20, 1992.

Address reprint requests to Dr Tatebe, Department of Thoracic and Cardiovascular Surgery, Niigata University School of Medicine, 757 Asahimachi-Dohri 1, Niigata City, 951, Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

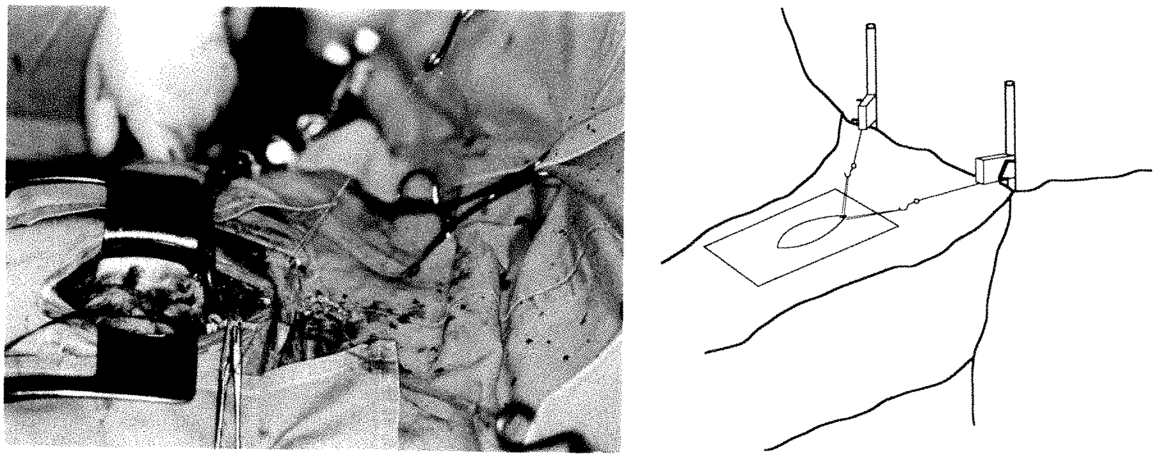


Fig 1. Use of a limited vertical skin incision for median sternotomy. The superior border of the skin incision was extended using braided silk sutures with felt pledgets attached to a mechanical scapular retractor. Exposure was adequate to use the sternal saw and accomplish aortic cannulation without difficulty.

and the top of the scar was not visible when patients wore a dress (Fig 2). No complications were attributable to the limited vertical skin incision.

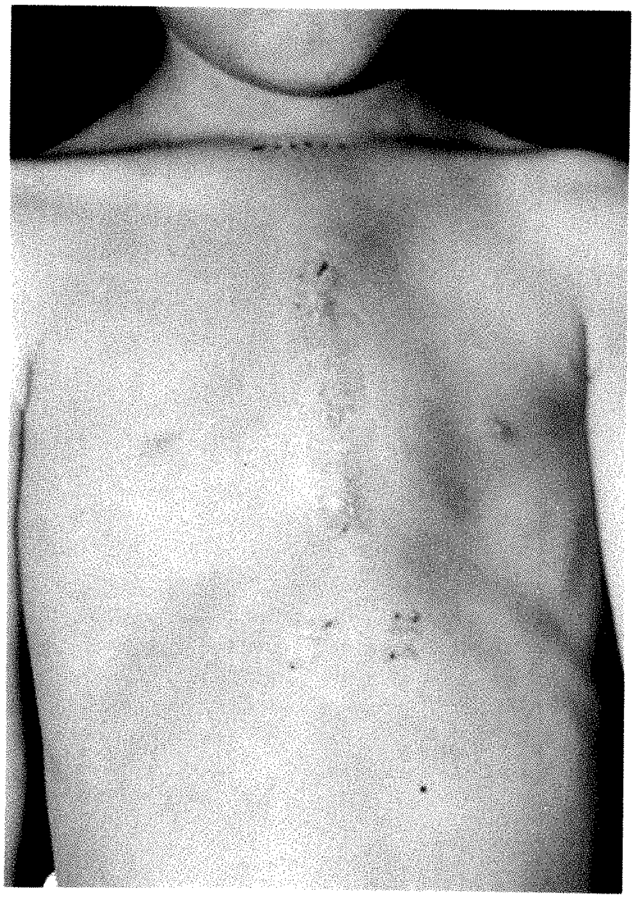


Fig 2. A representative patient after operation (5-year-old boy with atrial septal defect). The dotted line *indicated the point of sternal notch.*

Comment

Median sternotomy is widely used in cardiac operations. However, the vertical skin incision leaves an unattractive scar, which is visible when a woman wears a low-neck dress. This cosmetic deformity is particularly upsetting to young women.

There were attempts to use rubber tubing for traction of the skin to obtain a better exposure in a limited vertical skin incision with median sternotomy, but they were unsuccessful because of the rubber stretch. Our method uses a braided-silk suture, which permits greater tension. Our skin traction system is simple and useful, and lessens the cosmetic deformity associated with cardiac operations by permitting the use of a limited vertical skin incision.

We used this method in 7 patients with atrial septal defect or ventricular septal defect, as patients with atrial or ventricular septal defects are free from reoperation. Presently the indication for limited vertical skin incision using a mechanical skin traction system is considered to be congenital heart disease that is free from reoperation such as atrial septal defect, ventricular septal defect, and tetralogy of Fallot. In this trial, aortic cannulation was easily performed, but it was difficult to maneuver the distal aorta and distal pulmonary artery. Therefore, operations that require maneuvering of the distal aorta and distal pulmonary artery such as the arterial switch operation or Rastelli's operation are to be excluded.

References

1. Laks H, Hammond GL. A cosmetically acceptable incision for the median sternotomy. J Thorac Cardiovasc Surg 1980;79:146–9.
2. Martinez-Sanz R, Fleitas MG, de la Llana R, et al. Submammary median sternotomy. J Cardiovasc Surg 1990;31:578–80.
3. Bédard P, Keon WJ, Brais MP, Goldstein W. Submammary skin incision as a cosmetic approach to median sternotomy. Ann Thorac Surg 1986;41:339–41.

Directed Atraumatic Coronary Sinus Cannulation for Retrograde Cardioplegia Administration

Gabriel S. Aldea, MD, Gilbert Connelly, MD, James D. Fonger, MD,
Dusan Dobnick, MD, and Richard J. Shemin, MD

Departments of Cardiothoracic Surgery and Cardiac Anesthesia, Boston University Medical Center, Boston, Massachusetts

A simple method of coronary sinus cannulation for retrograde cardioplegia administration is described that reduces cardiac manipulation. Intraoperative transesophageal echocardiography is used to direct atraumatic coronary sinus cannulation, confirm the depth of insertion of the cannula tip in relation to the ostium, and reduce overall cannulation time.

(Ann Thorac Surg 1992;54:789–90)

Coronary sinus retrograde cardioplegia (CSRP) enhances antegrade myocardial protection by decreasing the inhomogeneous distribution and cooling of antegrade cardioplegia delivery beyond coronary artery obstructions [1–5]. The risk of coronary artery ostial injuries that may result from repeated ostial intubation during antegrade cardioplegia delivery in open aortic root procedures is eliminated by this technique [6]. Coronary sinus retrograde cardioplegia is also an alternative route for cardioplegia delivery when antegrade root cardioplegia with aortic insufficiency results in left ventricular distention. Coronary sinus retrograde cardioplegia is therefore applicable in a broad range of cardiac procedures. Initial concerns about trauma to the coronary sinus (CS) have been addressed by advances in catheter design and insertion techniques using a transatrial insertion with a flexible stylet. Myocardial edema is minimized by controlled delivery of cardioplegia at safe perfusion pressures of less than 40 mm Hg. Distal embolization of atheromatous graft debris in coronary reoperations may result from either antegrade cardioplegia delivery or the cardiac manipulation and dissection required for CSRP cannula insertion. This complication can be eliminated by inducing retrograde cardioplegic arrest using a "blind, no-touch" technique before cardiac dissection [7]. Despite these advances, trauma to the CS, improper catheter position, cannula dislodgment, and the extra time required for insertion are concerns that continue to limit the broad application of CSRP.

Intraoperative transesophageal echocardiography is extremely useful in directing the diagnosis and intraoperative management of valvular and ascending aortic operations. It is a particularly sensitive tool in demonstrating regional myocardial dysfunction that often precedes a decrease in cardiac output or electrocardiographic abnormalities [8, 9]. Transesophageal echocardiography can also image ascending aortic calcifications and direct the site selection for safe aortic root cannulation [10]. We therefore try to employ transesophageal echocardiography in all our cardiac operations.

Material and Methods

One hundred sixty-one consecutive patients underwent CSRP cannulation (Gundry CSRP cannula; DLP Inc, Grand Rapids, MI). The CSRP cannula was inserted through a pursestring in the right atrial wall and manually directed into the CS ostia before the initiation of cardiopulmonary bypass [6, 7]. Transesophageal echocardiographic guidance was used whenever available, and directed the CS cannulation in 71 of 161 patients. A single-plane 5.0-MHz transesophageal echocardiographic Hewlett-Packard probe was advanced to approximately 35 cm. With the scope retroflexed, the CS was visualized in all 71 patients in the horizontal plane, and tracked from the ostium across the lateral wall of the left ventricle. The CSRP cannula was easily distinguished from the pulmonary artery catheter by its characteristic acoustic signature. Transesophageal echocardiographic imaging ensured an atraumatic cannulation of the CS (Fig 1), readily detected cannula misdirection into the inferior vena cava or right ventricle, and provided an accurate measurement of the cannula insertion depth into the CS. Correct cannula position was also confirmed by digital palpation and wedged CS pressures. At the end of bypass the final CSRP cannula position was again confirmed by transesophageal echocardiography.

Results

Coronary sinus cannulation for retrograde cardioplegia administration was successful in 155 of 161 patients (96.3%). Transesophageal echocardiography-directed CS cannulation was successful in all 71 patients (100%). All CS cannulation failures occurred in patients in whom transesophageal echocardiography was not used (6/90 or 6.6%), and more than half of these (4/6) occurred in reoperations. Cannulation was considered to be a failure after multiple, manually redirected, blind insertion attempts. These difficulties may have represented CS ostial anomalies. Six such anomalies were identified in the directed cannulation group and all were successfully

---

Accepted for publication June 5, 1992.

Address reprint requests to Dr Aldea, Department of Cardiothoracic Surgery, Boston University Medical Center, 88 East Newton, Boston, MA 02118-2398.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

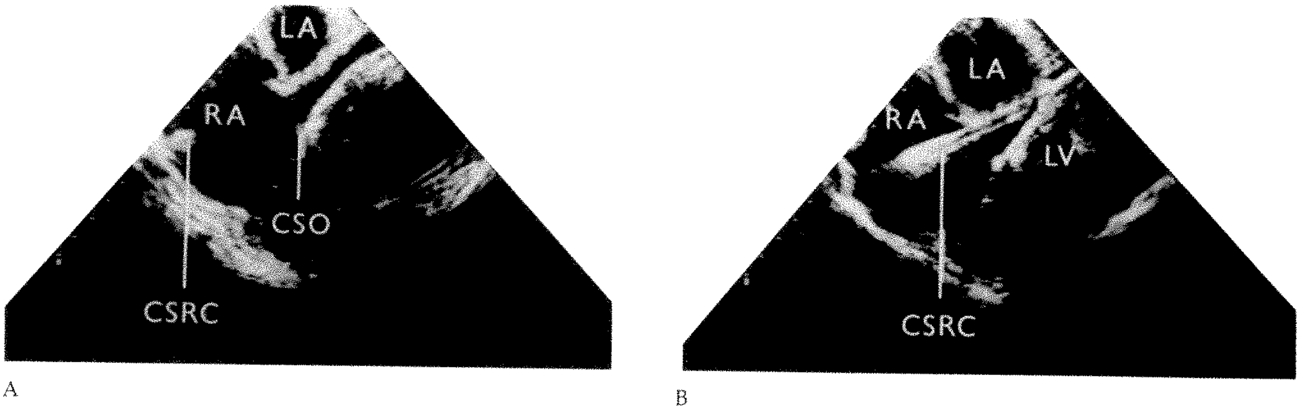


Fig 1. The four-chamber transesophageal echocardiographic view clearly visualizes the coronary sinus ostium (CSO), the right atrium (RA), the left atrium (LA), and the left ventricle (LV). (A) The coronary sinus retroperfusion cannula (CSRC) is seen to approach the CSO. (B) The CSRC is seen crossing the CSO in its final position.

crossed (four Eustachian valves, two separate origins of the posterior interventricular vein). In 20 of 71 patients (28%) the CSRP cannula was initially inserted too far and required readjustment to ensure optimal cardioplegia delivery. No injuries to the CS or catheter dislodgment after surgical manipulation occurred in either group. Transesophageal echocardiography-directed CS cannulation was completed in roughly one third the time required for blind insertion, with most directed insertions performed in less than 30 seconds.

Comment

Transesophageal echocardiography allows atraumatic cannulation of the CS, facilitates the proper positioning of the cannula tip, reduces insertion time, and minimizes cardiac manipulation before cardioplegic arrest.

References

1. Buckberg GD. Stategies and logic of cardioplegia delivery to prevent, avoid and reverse ischemic and reperfusion damage. J Thorac Cardiovasc Surg 1987;93:127–39.
2. Partington MT, Acar C, Buckberg GD, et al. Studies of retrograde cardioplegia. I. Capillary blood flow distribution to the myocardium supplied by open and occluded arteries. J Thorac Cardiovasc Surg 1989;97:605–12.
3. Partington MT, Acar C, Buckberg GD, et al. Studies of retrograde cardioplegia. II. Advantages of antegrade/retrograde cadioplegia to optimize distribution in jeopardized myocardium. J Thorac Cardiovasc Surg 1989;97:613–22.
4. Salerno TA, Houch JP, Barrozo LAM, et al. Retrograde continous blood cardioplegia: a new concept in myocardial protection. Ann Thorac Surg 1991;51:245–7.
5. Drinkwater DC, Laks H, Buckberg GD. A new simplified method of optimizing cardioplegic delivery without right heart isolation. J Thorac Cardiovasc Surg 1990;100:56–64.
6. Menasche P, Piwnica A. Cardioplegia by way of the coronary sinus for valvular and coronary surgery. J Am Coll Cardiol 1991;18:628–36.
7. Gundry SR, Razzouk AJ, Vigessa RE, et al. Optimal delivery of cardioplegic solution for "redo" operations. J Thorac Cardiovasc Surg 1992;103:896–1.
8. Smith JS, Cahalan MK, Benefiel DJ, et al. Intra-operative detection of myocardial ischemia in high-risk patients: electrocardiography versus two dimentional echocardiography. Circulation 1985;72:1015–21.
9. Battler A, Froelicher VF, Gallagher KP, et al. Dissociation between regional myocardial dysfunction and ECG changes during ischemia in the conscious dog. Circulation 1980;62:735–44.
10. Wareing TH, Davila-Roman VG, Barzilai B, Murphy SF, Kouchoukos NT. Management of the severely atherosclerotic aorta during cardiac operations. A strategy for detection and treatment. J Thorac Cardiovasc Surg 1992;103:453–62.

Bilateral Anterior Thoracotomy for Automatic Implantable Cardioverter Defibrillator Placement in Patients With Previous Sternotomy

Shreekanth V. Karwande, MD, and John R. Rowles, MD

Division of Cardiothoracic Surgery, Department of Surgery, University of Utah Medical Center, Salt Lake City, Utah

Bilateral anterior thoracotomy, extrapericardial patches, and endocardial sensing lead placement have been used in 40 patients with previous sternotomy. The mean defibrillation threshold was 15 J, and in all patients the defibrillation threshold was less than 20 J. The surgical procedure is simplified with less risk by avoiding dissection of previously operated regions. Serious pulmonary complications have been avoided by adequate pain control with epidural analgesia and early mobilization. This technique has successfully been used in patients with underlying chronic obstructive pulmonary disease and amiodarone-induced pulmonary fibrosis. All patients have been extubated by the first postoperative day.

(Ann Thorac Surg 1992;54:791–3)

Automatic implantable cardioverter defibrillators have emerged as an effective tool in the management of patients with life-threatening ventricular arrhythmias refractory to drug therapy. Mirowski and associates [1] implanted the first automatic implantable cardioverter defibrillator in a human in 1980.

The majority of patients requiring automatic implantable cardioverter defibrillator placement have ischemic cardiac disease and many have had a prior cardiac operation through a median sternotomy. Anterior-posterior placement of patch electrodes is difficult because of pericardial adhesions, and the risk of injury to adherent patent coronary bypass grafts is present. Extrapericardial patch lead placement has substantial advantages over epicardial placement. Intrapericardial dissection of previously operated regions is avoided and the risk of coronary artery bypass graft compression or erosion is minimized. In addition, ventricular compliance may be reduced with epicardial placement and subsequent scar formation. Extrapericardial patch leads have been as effective as epicardial placement with respect to energy requirements for successful termination of ventricular fibrillation in a canine model with experimentally induced pericardial adhesions and thickening [2].

From December 1986 to February 1992 we have used bilateral anterior thoracotomy, extrapericardial patches, and endocardial sensing lead placement in 40 patients at the University of Utah Medical Center with a prior history of sternotomy.

Technique

A lumbar epidural catheter is placed before the induction of general anesthesia or at the completion of the procedure for postoperative analgesia. Perioperative prophylactic antibiotics are used in all patients. The patient is placed supine on the operating table and the skin is prepared from the chin to the iliac crests. A single-lumen endotracheal tube is used for general anesthesia. A small incision inferior to the left midclavicle is made, and a right ventricular endocardial sensing lead is placed through the left subclavian vein using a modified Seldinger technique with fluoroscopic guidance (Fig 1A). Two operating teams perform simultaneous bilateral anterior thoracotomies through the fifth intercostal space for extrapericardial patch lead placement (Figs 1B, 1C). Dissection of extrapericardial fat is not done unless it is necessary for direct pericardial placement of anchoring sutures. A large patch lead is placed on the left ventricle around the apex and secured with four interrupted nonabsorbable sutures at each corner (see Fig 1B). The patch can be placed straddling the phrenic nerve, which is always identified and carefully avoided. A large patch is placed outside the pericardium adjacent to the right atrium anterior to the phrenic nerve and secured in a similar manner (Fig 1C). A transverse abdominal incision inferior to the left costal margin is made and a pocket developed in the subcutaneous space anterior to the rectus sheath (Fig 1D). Particular attention to hemostasis is necessary to minimize the risk of hematoma formation. All leads are tunneled subcutaneously to the left upper quadrant pocket using a chest tube as a guide. Standard intraoperative testing is performed to assure defibrillation thresholds of 20 J or less [3]. A 28F chest tube is placed in each pleural space. The ribs are reapproximated with two paracostal figure-of-8 polypropylene sutures, and all incisions are closed in layers with absorbable suture. Because of the incidence of perioperative supraventricular arrhythmias the device is not activated until the patient is transferred from the surgical intensive care unit to reduce the risk of unnecessary discharges. The chest tubes are removed routinely on the first postoperative day.

Accepted for publication June 15, 1992.

Address reprint requests to Dr Karwande, Division of Cardiothoracic Surgery, University of Utah Medical Center, 50 North Medical Dr, Salt Lake City, UT 84132.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

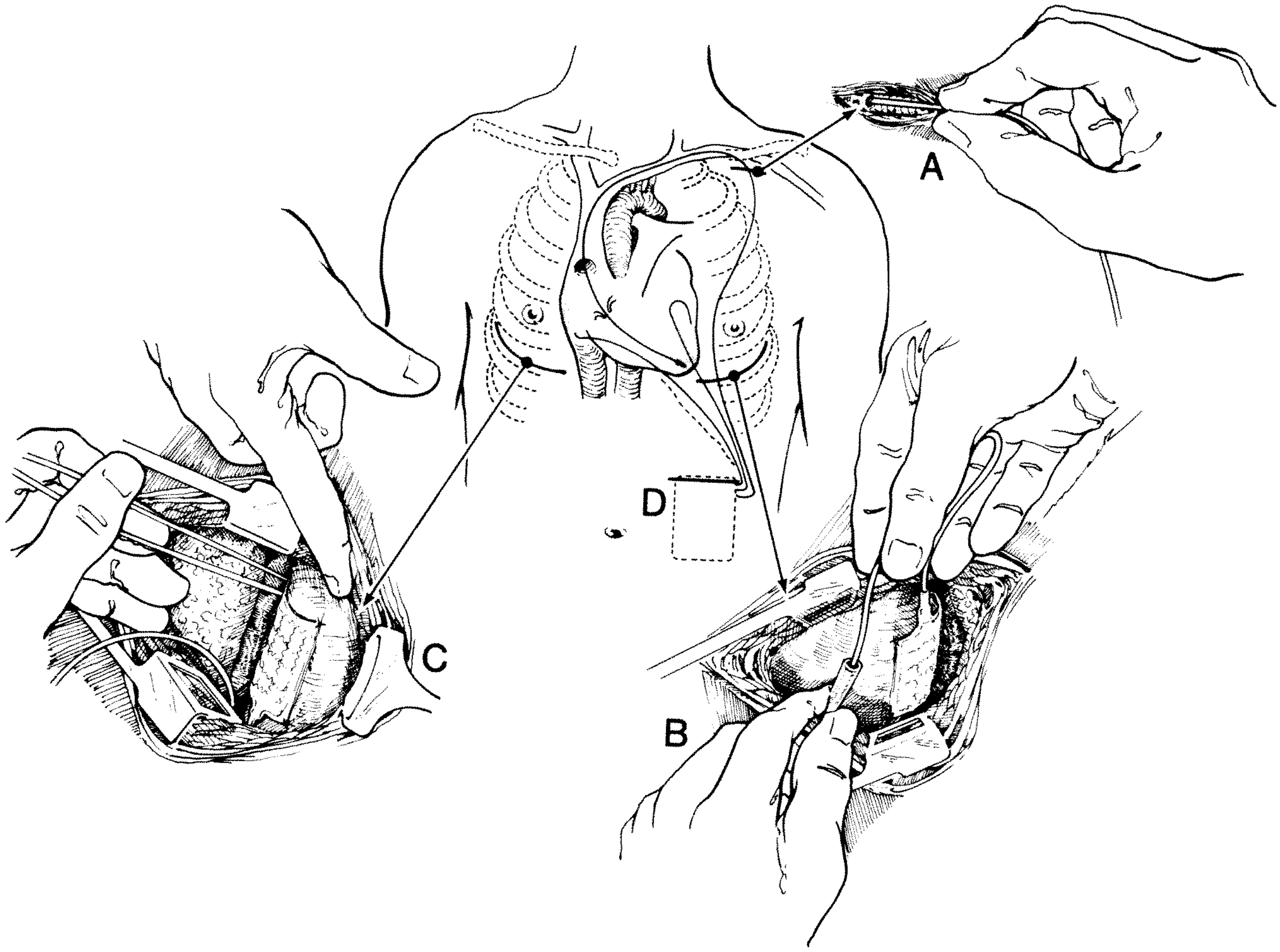


Fig 1. Operative technique for bilateral anterior thoracotomy and placement of extrapericardial patch lead and endocardial sensing lead. (A) Incision for the right ventricular endocardial sensing lead through the left subclavian vein. (B) Left anterior thoracotomy and extrapericardial patch lead placement over the left ventricular apex. (C) Right anterior thoracotomy and extrapericardial patch lead placement adjacent to the right atrium. (D) Left upper quadrant incision and location of the automatic implantable cardioverter defibrillator generator.

Comment

The most common technique for patch lead placement in patients with previous sternotomy has involved a left thoracotomy and anterior-posterior placement of patches. The anterior dissection is difficult because of scar, and the risk of injury to adherent coronary artery bypass grafts is present. In addition, defibrillation thresholds may be higher with anterior-posterior patch lead placement [4].

Extrapericardial patch lead placement reduces the risk of epicardial or coronary artery bypass graft erosion. Right ventricular perforation has been described with epicardial placement [5]. Ventricular compliance and diastolic filling may be adversely altered with epicardial patch leads and resultant scar formation. In addition, subsequent coronary artery bypass grafting is complicated by the dense fibrous tissue reaction beneath the epicardium and patches.

Bilateral anterior thoracotomy allows optimal extrapericardial patch lead placement and may be performed quickly with two operating teams. The mean defibrillation threshold was 15 J, and the threshold was less than 20 J in all patients in this series. Postoperative pain is well controlled with epidural analgesia for 5 to 7 days. If the catheter becomes dislodged or malfunctions, it is replaced. Other invasive catheters are removed as early as possible to facilitate mobilization and improve respiratory mechanics. Incentive spirometry is used routinely; bronchodilator therapy and chest physiotherapy are used when indicated. This technique has been successfully used in patients with chronic obstructive pulmonary disease as well as those with amiodarone-induced pulmonary fibrosis. All patients have been extubated by the first postoperative day. Clinically significant pleural effusions have not occurred in any patient.

This approach has simplified the placement of patch leads by avoiding dissection of previously operated regions without increasing pulmonary complications. Epidural analgesia for adequate pain control and early mobilization are important in the postoperative management of these patients.

References

1. Mirowski M, Reid PR, Mower MM, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. N Engl J Med 1980;303:322–4.
2. Lemmer JH, Faber LA, Mariano DJ, Drews TA, Kienzle MG, Behrendt DM. Pericardial influence on internal defibrillation energy requirements. J Thorac Cardiovasc Surg 1991;101:839–42.
3. Marchlinski FE, Flores B, Miller JM, Gottliers DC, Hargrove WC. Relation of the intraoperative defibrillation threshold to successful postoperative defibrillation with an automatic implantable cardioverter defibrillator. Am J Cardiol 1988;62:393–8.
4. Lawrie GM, Kaushik RR, Pacifico A. Right mini-thoracotomy: an adjunct to left subcostal automatic implantable cardioverter defibrillator implantation. Ann Thorac Surg 1989;47:780–1.
5. Sidari F, Klein H, Troster J. Intraventricular migration of an ICD patch. PACE 1990;13:1356–9.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1995 may begin the recertification process in 1993. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is May 1, 1993. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

New Side-Holed Sheath for Intraaortic Balloon Pumping to Maintain Limb Perfusion

Hisashi Satoh, MD, Tohru Kobayashi, MD, Taizou Hiraishi, MD, Makoto Sakurai, MD, Yoshiyuki Fudemoto, MD, Mitsunori Kaneko, MD, Susumu Nakano, MD, and Hikaru Matsuda, MD

Department of Cardiovascular Surgery, Center for Adult Diseases, and First Department of Surgery, Osaka University Medical School, Osaka, Japan

We developed a new side-holed shunt sheath for inserting intraaortic balloon pumps to maintain lower limb perfusion in patients with stenotic and tortuous aortoiliac arteries. This sheath has a large internal diameter and several side holes, which act as an internal shunt. It was useful and effective in 11 patients with severe aortoiliac occlusive lesions who required assistance by intraaortic balloon pumping.

(Ann Thorac Surg 1992;54:794–6)

Since Bregman and Casarella [1] introduced the percutaneous insertion method for intraaortic balloon pumping (IABP), the indications for IABP have been extensively widened. However, the problems of vascular complications, especially limb ischemia during balloon pumping, remained unsolved. We devised a new side-holed sheath to maintain lower limb perfusion in patients with severe aortoiliac occlusive lesions who require assistance by IABP.

Instrument and Method

To create the side-holed IABP shunt sheath, several holes were made in the side of a commercially available sheath with a large inner diameter. The sheath serves as an internal shunt of the blood flow to the distal side of the stenotic lesion through the gap between the sheath and the balloon catheter and the side holes (Fig 1). This sheath is 12F in diameter and 25 cm long so that it can be inserted as far as the abdominal aorta. Ten side holes 2 mm in diameter are made along the sheath from 1 cm to 19 cm from the tip. The inner diameter of the sheath is 4.17 mm and the outer diameter, 4.77 mm. When a balloon catheter of 10F or less is used, it is possible to maintain the blood flow through the gap between the inside of the sheath and the distal side holes. At the end of the sheath, a hemostatic valve is provided to prevent bleeding during insertion of the catheter. A side port is attached for arterial pressure measurement and injection of drugs (Fig 2). This side-holed IABP shunt sheath can be inserted by the conventional Seldinger method, like a standard sheath. After the femoral artery is punctured, it is dilated with an 8F predilator, and the side-holed IABP sheath and a 12F dilator are inserted using the 0.035-inch or 0.032-inch 150-cm guidewire.

This side-holed IABP shunt sheath was used in 11 patients postoperatively (coronary bypass grafting in 4 patients, coronary angioplasty in 6, and closure of a ventricular septal defect in 1 patient). The ages ranged from 58 to 79 years with a mean age of 67 years. Eight patients were male and 3, female. The duration of balloon pumping ranged from 4 to 192 hours (average, 81 hours). All patients had undergone aortoiliac angiography at the time of the diagnostic cardiac catheterization, and angiographically stenotic and tortuous lesions were demonstrated in each patient. In 6 patients, the sheath was inserted under fluoroscopy; in 5 patients insertion was done without use of a fluoroscope. All patients underwent a percutaneous approach with the side-holed IABP shunt sheath. A Kontron 8.5F, 30-mL balloon catheter was used in 9 patients and a Datascope 9.5F, 36-mL balloon catheter in 2 patients.

Results

While this side-holed IABP shunt sheath was being used, the distal lower-extremity pulse was well palpated on the side of insertion. No temperature differences between the lower limbs were found. The ankle/brachial pressure index was maintained at about 0.6 to 0.8, and good lower limb perfusion was maintained by the internal shunt. No complications due to the use of this side-holed IABP shunt sheath occurred in any of the 11 patients.

In a 72-year-old woman with cardiogenic shock due to a ventricular septal defect after acute myocardial infarction, the angiogram showed both iliac arteries to be markedly tortuous (Fig 3). A conventional sheath (Datascope, 11.5F outer diameter) was inserted. The external iliac artery was completely obstructed by the sheath (Fig 4), so it was exchanged with the side-holed IABP shunt sheath. The distal femoral artery was imaged from the side holes at the

---

Accepted for publication June 29, 1992.

Address reprint requests to Dr Matsuda, First Department of Surgery, Osaka University Medical School, 1-1-50 Fukushima, Fukushima-ku, Osaka, 553 Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

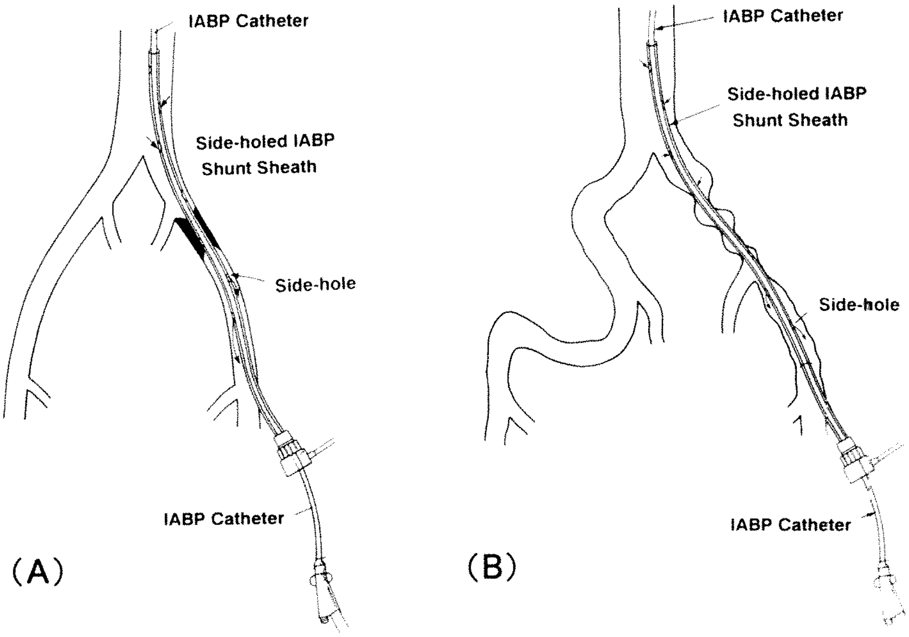


Fig 1. Side-holed intraaortic balloon pump (IABP) shunt sheath for stenotic (A) and tortuous (B) lesions of the aortoiliac artery.

end of the obstruction by the contrast medium, which flowed into the gap inside the sheath (see Fig 4).

Comment

In recent years, various improvements have been made in IABP systems, including the use of wire-guided and finer sized balloon catheters. However, there have been many reports concerning vascular complications during balloon pumping [1–4]. The complications depend on the severity of the lower limb ischemia on the side of insertion [5, 6]. Atherosclerotic lesions and a tortuous aortoiliac arterial tree were mainly responsible for the vascular complications [3]. We observed major vascular complications in 3 patients (3%) suffering from lower limb ischemia among 102 patients who had undergone a percutaneous approach with a conventional IABP system.

We devised the side-holed IABP shunt sheath to reduce the risk of lower limb ischemia during balloon pumping. The side holes serve as an internal shunt for the blood flow to the distal part of the stenotic region through the gap between the large inner diameter sheath and the finer sized IABP catheter (see Figs 3, 4). In 11 patients with stenosis or tortuous lesions of the aortoiliac artery, this sheath effectively maintained lower limb perfusion during balloon pumping and was useful in the critically ill patients. No complications due to the use of this side-holed IABP shunt sheath occurred in any of the patients. It was possible to confirm the perfusion from the aortoiliac artery to the femoral artery by contrast medium injected through the side port of the sheath at the bedside after the placement of the IABP.

Thus, the side-holed IABP shunt sheath appears to be useful and capable of effectively maintaining lower limb perfusion, even in patients with severe aortoiliac occlusive lesions.

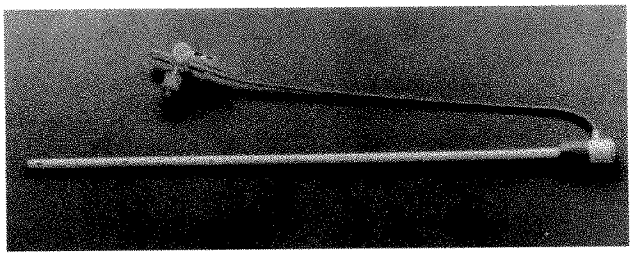


Fig 2. Side-holed intraaortic balloon pump shunt sheath (12F, 25-cm sheath with ten side holes, hemostatic valve, and side port).

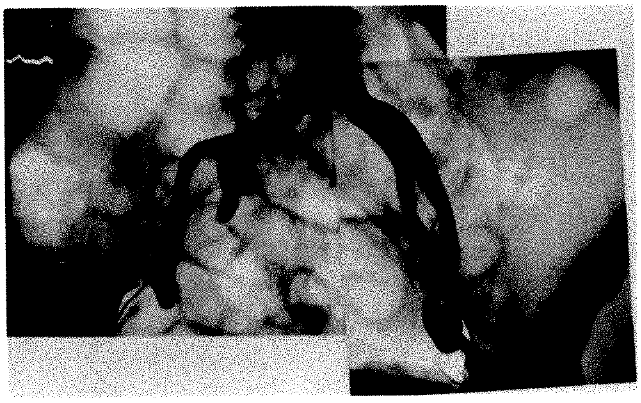


Fig 3. Aortoiliac angiogram showing marked tortuousity of the iliac arteries.

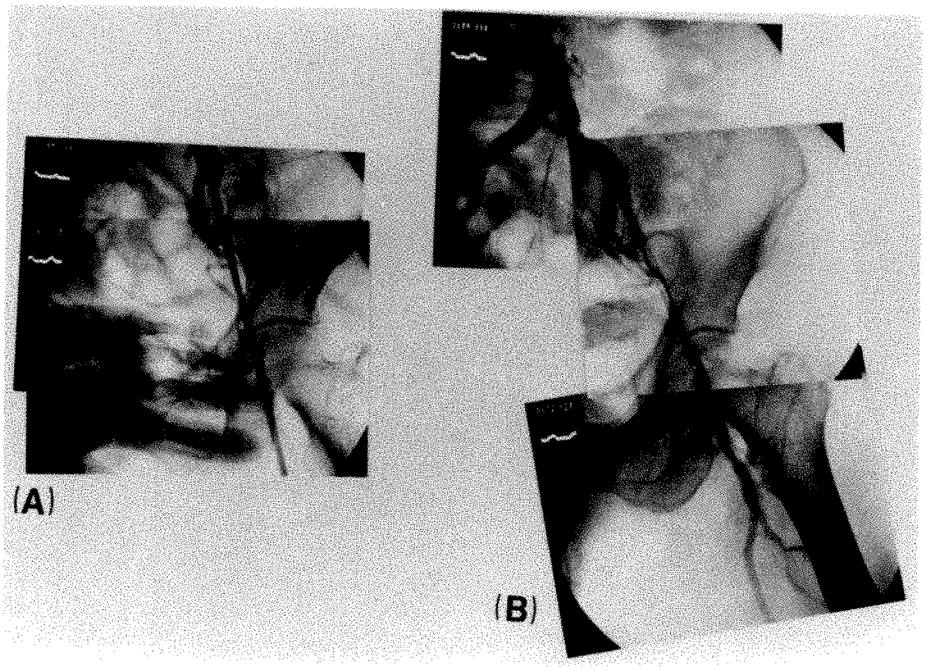


Fig 4. Aortoiliac angiogram showing the external iliac artery completely obstructed by a conventional sheath (A). The femoral artery was imaged with the side-holed intraaortic balloon pump shunt sheath (B).

References

1. Bregman D, Casarella WJ. Percutaneous intraaortic balloon pumping: initial clinical experience. Ann Thorac Surg 1980;29:153–5.
2. Alderman JM, Gabliani GI, McCabe CH, et al. Incidence and management of limb ischemia with percutaneous wire-guided intraaortic balloon catheters. J Am Coll Cardiol 1987;9:524–30.
3. Di Lello F, Mullen DC, Flemma RJ, Anderson AJ, Kleinman LH, Werner PH. Results of intraaortic balloon pumping after cardiac surgery: experience with the Percor balloon catheter. Ann Thorac Surg 1988;46:442–6.
4. Kantrowitz A, Wasfile T, Freed PS, et al. Intraaortic balloon pumping 1967 through 1982: analysis of complications in 733 patients. Am J Cardiol 1986;57:976–83.
5. Funk M, Gleason J, Foell D. Lower limb ischemia related to use of the intraaortic balloon pump. Heart Lung 1989;18:542–52.
6. Beckman CB, Geha AS, Hammond GL, et al. Results and complications of intraaortic balloon counterpulsation. Ann Thorac Surg 1977;24:550–9.

New Surgical Technique for Type B Aortic Interruption

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Fadel Al-Fadley, FRCP(C), Zohair Al-Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

Restoring continuity of the aortic arch in aortic interruption continues to be a problem in terms of both surgical technique and long-term results. We report here a surgical technique using the left subclavian artery along with an aberrant right subclavian artery to form a conduit in a patient with type B interruption, to reestablish aortic continuity.

(Ann Thorac Surg 1992;54:797–9)

Untreated interruption of aortic arch has an 80% mortality in the first month of life [1]. Repair of the arch interruption and associated cardiac anomalies may be undertaken in two stages when the interruption is corrected first, or by complete correction of all anomalies in one stage. In either case, establishing continuity of the proximal to the distal aorta continues to be a technical challenge. We describe a new technique to reestablish continuity of the aortic arch using both subclavian arteries in a type B interrupted aortic arch.

A 20-month-old female child was referred to our institute on discovery of a systolic murmur on routine examination for a respiratory tract infection. On examination her weight and height were normal for her age. There was no cyanosis, clubbing, or dyspnea. Peripheral pulses were normal with no radiofemoral delay. Auscultation revealed a grade 4/6 systolic murmur over the third intercostal space at the left sternal border.

Electrocardiogram showed left atrial enlargement and biventricular hypertrophy with right axis deviation. Echocardiogram and cardiac catheterization revealed hypoplastic ascending aorta, type B aortic interruption, and large patent ductus arteriosus with both left and right subclavian arteries arising from the descending aorta (Fig 1). The course of the right subclavian artery was retroesophageal. There was associated subaortic stenosis with a posterior malaligned ventricular septal defect of moderate size. The left ventricle was of normal size with good function.

The pulmonary artery pressure was high (87/49 mm Hg; mean, 66 mm Hg; pulmonary to systemic resistance ratio = 0.4), whereas the mean wedge pressure was 18 mm Hg. The gradient across the left ventricular outflow tract was 65 mm Hg, and there was a 60 mm Hg gradient across the ventricular septal defect (pulmonary to systemic blood flow ratio = 1.4:1).

It was decided to correct the aortic interruption as a first stage and evaluate the pulmonary vascular disease by lung biopsies with a view toward total correction of her cardiac anomalies at a later date.

Thoracotomy was performed through the fourth left intercostal space. The ascending aorta, descending aorta, carotid arteries and both subclavian arteries were fully dissected and mobilized. The ascending aorta, both carotid arteries, and both subclavian arteries were of a small caliber. There was a 2-cm interruption between the proximal aortic arch and distal aorta. The ascending aorta gave rise to the left and right common carotid arteries. The distal aorta was fed by a large ductus from the left pulmonary artery, and both subclavian arteries were found to be arising in close proximity from the descending aorta opposite the ductus. The right subclavian artery was confirmed to be retroesophageal in course.

In view of the existing arterial anatomy and the long segment interruption of aorta, which could not be bridged by mobilization of the segments for direct anastomosis, we elected to use both subclavian arteries in the repair. A side-biting vascular clamp was placed on the descending aorta encircling the origin of both subclavian arteries so as to permit distal flow in the descending aorta through the ductus. The subclavian arteries were ligated distally and a vertical arteriotomy was done on the facing surfaces of the two arteries meeting at the point of their origin (Fig 2, inset). They were sewn together with 6-0 PDS (Ethicon Ltd, Edinburgh, Scotland) to form a tube (see Fig 2). The open end of the subclavian tube was swung upward and anastomosed to the left common carotid artery using 7-0 PDS as the ascending aorta was too small to apply a vascular clamp with safety.

A trial occlusion of the ductus led to a drop in systemic blood pressure, and no further attempt was made to proceed with ductal ligation. There was no gradient across the subclavian tube. Multiple lung biopsies were performed on the left lung. Histologic examination showed type IIB (Edward Heath) pulmonary vascular changes. The child recovered normally from this first-stage correction.

Comment

Aortic arch interruption, which later came to be classified as type B [2], was first described in 1818 by Seidel [1]. In type B, the interruption occurs beyond the left common carotid artery. This is the most common type, accounting

---

Accepted for publication June 30, 1992.

Address reprint requests to Dr Prabhakar, MBC 16, King Faisal Specialist Hospital and Research Center, PO Box 3354, Riyadh 11211, Saudi Arabia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

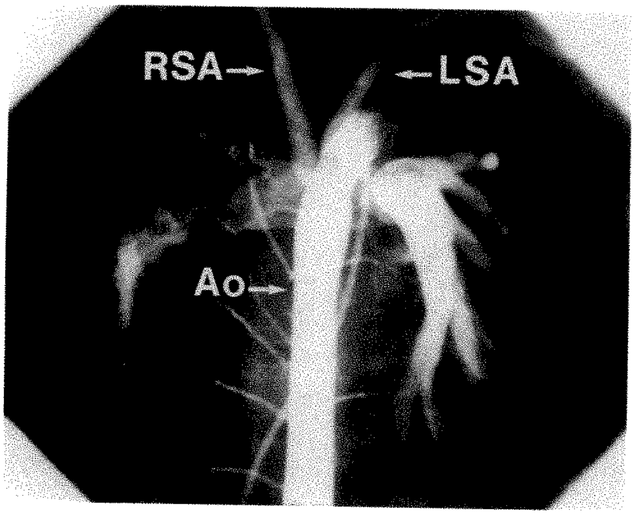


Fig 1. Angiogram (posteroanterior view) showing the distal segment of aorta (Ao) giving rise to the left subclavian artery (LSA) and the anomalous right subclavian artery (RSA) with normal pulmonary arterial distribution. The contrast injection was performed in the large patent ductus arteriosus from the right side of the heart.

for more than 53% of all interruptions [1]. This is not uncommonly associated with aberrant origin of the right subclavian artery from the descending aorta [3]. It is frequently associated with other intracardiac anomalies such as ventricular septal defects, transposition of the great arteries, truncus arteriosus, and aortic valvar stenosis [3]. Rarely does it form part of a developmental complex of ventricular septal defects, overriding pulmonary trunk, and subaortic stenosis [4].

Surgical palliation for type B aortic interruption was first achieved in 1957 [5] by anastomosing the ascending aorta to the left subclavian artery, and successful total correction in a single stage was performed in 1973 [6]. Improving results with one-stage correction [7] have led to its increasing use [8], whereas two-stage correction continues to be recommended by others until more long-term information is available [9–11].

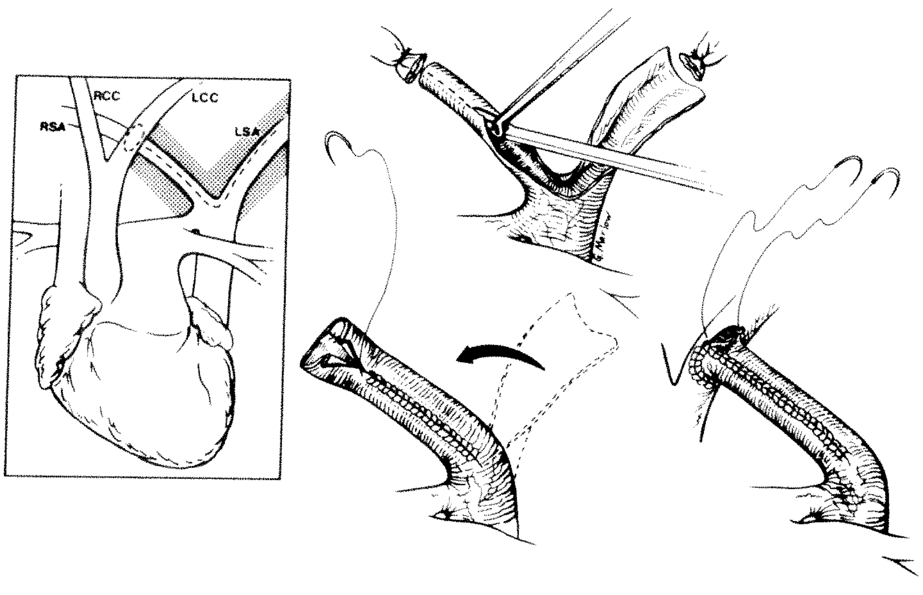
We normally employ one-stage correction through a median sternotomy. This was not used in this patient in view of the high pulmonary artery pressure. It was considered that preliminary restoration of aortic continuity with ductal ligation would improve the overall success as this would also permit study of the pulmonary vascular disease. However, ductal ligation could not be carried out as trial occlusion led to hemodynamic decompensation. This could be due to a combination of severe subaortic obstruction and the small size of the aorta. It was believed that the ductus was shunting right to left and was providing an outlet in the presence of this severe left ventricular outflow tract obstruction. Ductal patency may preclude the future growth of aortic arch in this child. Pulmonary vascular changes with reversal of shunt mitigating ligation of the ductus arteriosus could not be ruled out.

Independent of whether a one-stage or two-stage correction is employed, restoration of aortic continuity is a major problem in terms of both surgical technique and long-term results [7, 10], especially for long-segment interruptions of the aorta in older children.

The ascending aorta is usually small and straight [12], and applying a side-biting vascular clamp to it can be difficult [13]. In our patient it was difficult to apply a proximal clamp due to the small size of the aorta, leading us to anastomose the subclavian artery tube to the left common carotid artery. What is not usually mentioned in literature is that clamping the descending segment of the aorta can also be difficult because the clamp tends to encroach on the ductus arteriosus, increasing the stress on the left ventricle and leading to its decompensation.

Continuity of the interrupted aorta can be restored by direct anastomosis of the ascending to the descending aorta or by bridging the gap with prosthetic tubes, a homograft, or the patient's own tissues. One-stage correction of all cardiac anomalies, including subaortic ste-

Fig 2. Schematic illustration of the surgical technique. (LCC = left common carotid artery; LSA = left subclavian artery; RCC = right common carotid artery; RSA = right subclavian artery.)



nosis using homografts, has been reported [14]. Direct anastomosis by extensive mobilization is possible in an infant with a short-segment interruption, but this might prove impossible in an older child [12]. In view of the small size of the anastomosis it may have to be extended onto the carotid artery [8]. Murphy and associates [6] used a vein graft from the parents of the child to bypass the interruption, whereas most others use prosthetic materials such as Teflon [1], Dacron [15], or polytetrafluoroethylene grafts [10].

A left carotid artery turndown procedure, anastomosing it to the aorta, may be performed [16, 17]. Ductus arteriosus [18] or a left subclavian artery turnup has been used [19] for bridging the gap. Whatever the method that is employed for restoration of aortic continuity, the single most important factor is to avoid tension as this may cause late stenosis [17].

Children tend to outgrow their grafts by 7 to 10 years of age, even when 8- to 10-mm polytetrafluoroethylene conduits are used. They have a further disadvantage in that balloon dilation is not useful in cases of graft stenosis [10].

Direct anastomosis was not possible in our patient due to a long-segment interruption, small ascending aortic size, inability to tolerate even minor occlusion of the ductus, and older age compared with other series [7]. In a review of results of a surgical program for interrupted aortic arch of 71 patients, only 3 patients were over the age of 1 year at the time of entry into the study. A carotid turndown was not used in our patient due to the small size of the artery. Each of the subclavian arteries was also too small to be used by itself if gradients were to be avoided. Combining the two subclavian arteries provided an ideal conduit and also eliminated the need to clamp a large portion of the descending aorta. Turning the subclavian artery tube upward and anastomosing it to the carotid artery avoided compromise of the ascending aortic lumen with vascular clamps.

In conclusion, we report a new palliative surgical technique using both subclavian arteries in an older child with type B aortic interruption associated with intracardiac anomalies.

We are grateful to Gregory Marlow for the medical illustrations and Alison Silkstone for her help in the preparation of the manuscript.

References

1. Van Praagh R, Bernhard WF, Rosenthal A, Parisi LF, Fyler DC. Interrupted aortic arch: surgical treatment. Am J Cardiol 1971;27:200–11.
2. Celoria GC, Patton RB. Congenital absence of the aortic arch. Am Heart J 1959;58:407–13.
3. Moller JH, Edwards JE. Interruption of aortic arch. Anatomic patterns and associated cardiac malformations. AJR 1965;95:557–72.
4. Becu LM, Tauxe WN, DuShane JW, Edwards JE. A complex of congenital anomalies: ventricular septal defects, biventricular origin of pulmonary trunk, and subaortic stenosis. Am Heart J 1955;50:901–11.
5. Merrill DL, Webster CA, Samson PC. Congenital absence of the aortic isthmus. Report of a case with successful surgical repair. J Thorac Surg 1957;33:311–20.
6. Murphy DA, Lemire GG, Tessler I, Dunn GL. Correction of type B aortic arch interruption with ventricular and atrial septal defects in a three-day-old infant. J Thorac Cardiovasc Surg 1973;65:882–6.
7. Sell JE, Jonas RA, Mayer JE, Blackstone EH, Kirklin JW, Castaneda AR. The results of a surgical program for interrupted aortic arch. J Thorac Cardiovasc Surg 1988;96:864–77.
8. Hammon JW Jr, Merrill WH, Prager RL, Graham TP Jr, Bender HW Jr. Repair of interrupted aortic arch and associated malformations in infancy: indications for complete or partial repair. Ann Thorac Surg 1986;42:17–21.
9. Griffin S, Richens D, Behl R. Early results of direct repair of aortic interruption by the lateral approach. Ann Thorac Surg 1992;53:430–4.
10. Irwin ED, Braunlin EA, Foker JE. Staged repair of interrupted aortic arch and ventricular septal defect in infancy. Ann Thorac Surg 1991;52:632–9.
11. Sawin RS, Hall DG, Mansfield PB, Rittenhouse EA. Staged repair of interrupted aortic arch with ventricular septal defect compared with primary repair in infancy. Am J Surg 1989;157:487–9.
12. Trusler GA, Izukawa T. Interrupted aortic arch and ventricular septal defect. Direct repair through a median sternotomy incision in a 13 day old infant. J Thorac Cardiovasc Surg 1975;69:126–31.
13. Sirak HD, Ressallat M, Hosier DM, DeLorimier AA. A new operation for repairing aortic arch atresia in infancy. Circulation 1968;37,38(Suppl 2):43–50.
14. Clarke DR. Homografts for congenital heart disease. In: Kron IL, Mavroudis C, eds. Cardiac surgery: state-of-the-art reviews. Philadelphia: Hanley & Belfus, 1989:363.
15. Litwin SB, Van Praagh R, Bernhard WF. A palliative operation for certain infants with aortic arch interruption. Ann Thorac Surg 1972;14:369–75.
16. Quie PG, Novick R, Adams P, Anderson RC, Varco RL. Congenital interruption of the aortic arch. J Pediatr 1959;54:87–92.
17. Monro JL, Bunton RW, Sutherland GR, Keeton BR. Correction of interrupted aortic arch. J Thorac Cardiovasc Surg 1989;98:421–7.
18. Kawashima Y, Dyama C, Mori T, Manabe H. Interruption of the aortic arch associated with patent ductus arteriosus and ventricular septal defect. J Cardiovasc Surg 1975;16:426–31.
19. Fishman NH, Bronstein MH, Berman W, et al. Surgical management of severe aortic coarctation and interrupted aortic arch in neonates. J Thorac Cardiovasc Surg 1976;71:35–48.

Video-Assisted Thoracic Surgery: Basic Technical Concepts and Intercostal Approach Strategies

Rodney J. Landreneau, MD, Michael J. Mack, MD, Stephen R. Hazelrigg, MD,
Robert D. Dowling, MD, Tea E. Acuff, MD, Mitchell J. Magee, MD, and
Peter F. Ferson, MD

Section of Thoracic Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania; Division of Cardiothoracic Surgery, Humana Hospital, Dallas, Texas; and Division of Cardiothoracic Surgery, St. Luke's Medical Center, Milwaukee, Wisconsin

Video-assisted thoracic surgery is emerging as a viable approach to a number of intrathoracic disorders. Technical difficulties related to improper instrument selection and suboptimal intercostal operative access can reduce the utility of, and the enthusiasm for, the video-assisted thoracic surgical approach. This report describes the intercostal access strategy and the instrument positioning that we now prescribe for many video-assisted thoracic surgical procedures. These approaches have become refined during the course of our experience with 467 patients undergoing video-assisted thoracic operations over the last 18 months.

(Ann Thorac Surg 1992;54:800–7)

Improvements in video endoscopic surgical equipment and a growing enthusiasm for minimally invasive surgical approaches have fostered a resurgence of interest in thoracoscopy [1–6]. Over the last 18 months, we have expanded our use of thoracoscopic, or video-assisted thoracic surgical (VATS), procedures to address a variety of thoracic problems classically managed through open thoracotomy. To date, this experience involves 467 patients who have been successfully managed without operative mortality (Table 1).

The goal of this report is to assist thoracic surgeons beginning their thoracoscopic experience with the basic operative setup for thoracoscopic (VATS) surgery. In addition, we hope to provide insight into the proper intercostal positioning of endoscopic instruments and video equipment for their strategic use during the course of various VATS procedures.

Basic Operative Setup and Procedure

The VATS approach requires an appropriate operating room environment that allows the thoracic surgeon the immediate potential to convert to an open thoracotomy if necessary. The basic operative setup includes the following:

General anesthesia
Double-lumen endotracheal tube (or bronchial blocker)
Open thoracotomy instrument tray available (? open on back table)
Thoracoscope (10-mm operative scope preferred with a 5-mm operative channel)
High-resolution video monitor (×2) (two monitors preferably positioned on opposite sides of the operating table for the surgeon and assisting team)
Two to five ports of intercostal operative access
Videoscopic instruments (and selected standard surgical instruments)
Endoscopic stapling and clip appliers (neodymium:yttrium-aluminum garnet laser is useful adjunct during resection)
Adequate suction and smoke evacuation system

It is also important to assemble an operative team that is familiar with standard thoracic surgical procedures. Anesthesia personnel should be experienced in open thoracic procedures and well versed in the principles of selective one-lung ventilation [1, 7, 8].

Video-assisted thoracic surgical procedures should be performed in an orderly and sequential fashion [9, 10]. The patient is positioned in a full lateral position with the thorax surgically prepared in case conversion to an open thoracotomy is necessary during the course of the operation. We begin the VATS procedure by choosing an appropriate intercostal site of access for exploratory thoracoscopy. Sharp dissection and direct digital exploration are used to rule out local pleural adhesions that can impede the introduction of instruments and potentially result in pulmonary parenchymal injury (Fig 1). Flimsy local adhesions can often be digitally separated, but the presence of more extensive pleural symphysis may necessitate alternative intercostal access to conduct thoracoscopy. If extensive pleural fusion is found, the thoracoscopic procedure is aborted, and conversion to an open thoracotomy is chosen.

We usually rely on the sixth to seventh intercostal space (ICS) in the midaxillary to posterior axillary line for trocar-protected thoracoscopic access to the pleural cavity. This location commonly provides an unobstructed panoramic view of the entire hemithorax. Trocar protection is

---

Address reprint requests to Dr Landreneau, Section of Thoracic Surgery, University of Pittsburgh, Montefiore University Hospital, 3459 Fifth Ave, Pittsburgh, PA 15213.

© 1992 by The Society of Thoracic Surgeons

Table 1. Thoracoscopic Surgical Procedures in 467 Patients From December 1990 to March 1992

Procedure	No. of Patients
Pleural disease	112
Blebectomy	38
Lung resection	
Closed wedge biopsy	50
Wedge resection (nodule)	175
Lobectomy	9
Mediastinal mass resection	
Anterior	9
Posterior	4
Mediastinal biopsy	31
Pericardiectomy	22
Esophageal disease	
Myotomy (achalasia)	4
Leiomyoma	1
Thoracic duct ligation	1
Sympathectomy	10
AICD	1
Spinal disease	2

AICD = automatic implantable cardioverter defibrillator

required primarily to reduce smudging of the lens as the thoracoscope is introduced into the chest. Exploratory thoracoscopy is then performed. The relatively inferior and posterior initial intercostal placement of the thoracoscope assists us in maintaining our intrathoracic orientation as we view the mediastinum, the lung surface, the major pulmonary fissures, and the area over the apex of the lung. We have been impressed with the visibility achieved with the VATS approach. This contrasts with the limited visibility frequently obtained through an axillary, inframammary, or lateral thoracotomy [11]. After the initial thoracoscopic exploration of the pleural cavity is concluded, further intercostal access for VATS instrumentation is accomplished under direct thoracoscopic vision (Fig 2).

Carbon dioxide insufflation is not a necessity for successful thoracoscopic operations. We do, however, frequently introduce carbon dioxide into the thorax at the beginning of the procedure to facilitate a more complete and expeditious collapse of the lung. The intrapleural pressure is measured and kept lower than 10 mm Hg to avoid mediastinal tension and hemodynamic compromise. It is necessary to use air-tight valved (reusable or disposable) trocars to seal the gas within the thorax when this carbon dioxide insufflation technique is used.

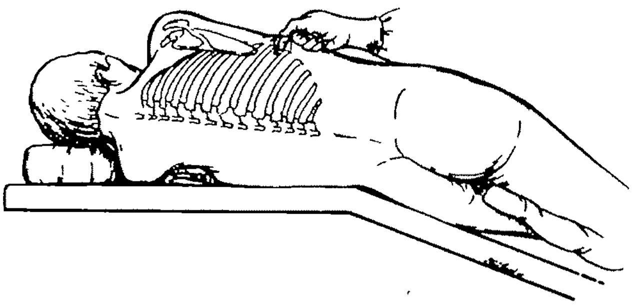


Fig 1. Patient in the right lateral decubitus position and digital exploration of the proposed initial trocar site to ensure that a free pleural space is present.

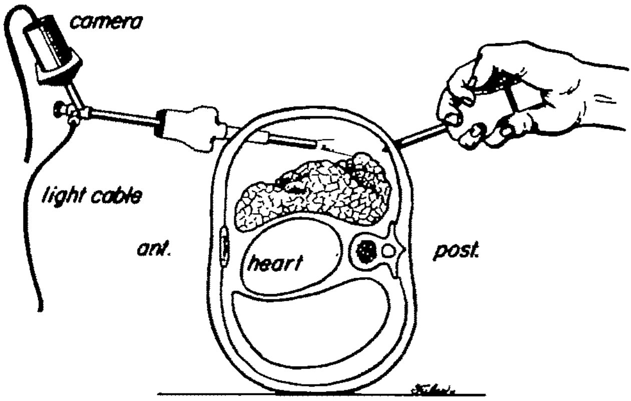


Fig 2. Secondary trocar sites being established under direct endoscopic visibility and direction to ensure proper location and avoid intercostal neurovascular bundle trauma.

To accomplish the basic maneuvers of thoracoscopy and to conduct effective VATS operations, several basic principles should be applied.

1. Place trocar sites and thoracoscope at a distance from the lesion to achieve a panoramic view and provide room to manipulate the tissue.
2. Avoid instrument crowding, which may otherwise result in "fencing" during instrument manipulation.
3. Avoid mirror imaging by positioning instruments and thoracoscope within the same 180-degree arc (approach the lesion in the same general direction with instruments and camera).
4. Move or manipulate instruments (or the camera) *serially*, rather than randomly or synchronously, to avoid operative chaos. Instruments should be manipulated only when seen directly through the thoracoscope.

The primary operative strategy is to orient the endoscopic instruments and the thoracoscopic camera so that all are being used in the same general direction—facing toward the target pathology (Fig 3). This will avoid awkward handling of instruments because of the mirror imaging that results when the instruments are pointed toward the thoracoscopic camera.

Strategic positioning of the thoracoscopic camera and the endoscopic instruments is vital to the success and efficiency of the procedure. Indeed, the person handling the camera has primary video control of the procedure. This camera operator, who may be an assistant or a primary surgeon, coordinates the manipulation of instruments used by all other surgeons and assistants. We emphasize that it is best for the surgical team to manipulate (or position) only a single instrument at a time to avoid operative chaos. The camera operator should direct

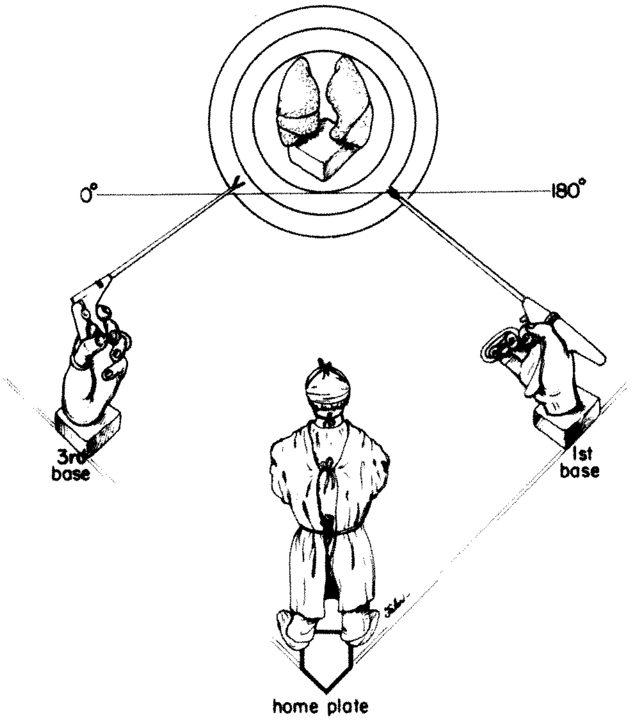


Fig 3. Baseball-diamond concept for triangulation of the instruments and thoracoscope for strategic visibility and manipulation of the target pathology.

his or her primary attention to the first maneuver of the procedure and assist in the alignment of all instruments necessary to accomplish it. Once that maneuver is completed, he or she will then coordinate the endoscopic view of the surgical team to the next step of the procedure.

We periodically retract the thoracoscope from a close-up (magnified) image of the intrathoracic target to obtain a panoramic view of the operative field and to confirm proper positioning of all intrathoracic instruments. We also use this scanning maneuver whenever an additional instrument is introduced into the thorax. The enhanced visualization of the target pathology is then regained once instrument alignment is achieved. We strongly encourage the use of antifogging agents (FRED; Dexide, Inc, Fort Worth, TX) and periodic warming of the shaft of the thoracoscope with hot saline solution to avoid the fogging of the thoracoscopic lens that tends to occur because of differences in the operating room ambient temperature and the temperature within the thorax.

Although disposable instruments and trocars are available from a variety of companies, we rely primarily on reusable endoscopic surgical instruments. There are some disposable endoscopic instruments (ie, endoscopic stapling devices and multiload endoscopic clip appliers) that have a uniquely important role in many VATS procedures. We also prefer the disposable endoscopic scissors because of the rapid dulling of currently available reusable endoscopic scissors. We believe that the current medical economic environment dictates judicious use of disposable endoscopic surgical instruments by active thoracoscopy programs.

For most VATS procedures, we prefer a 10-mm thoracoscope with a 5-mm operative channel, if available (Karl Storz Endoscopy-America, Inc, Olympus Corp, or Wolfe Endoscopic Inc), over the view-only laparoscopes. The 10-mm operative thoracoscope provides the opportunity for "single-stick" diagnostic thoracoscopy and potentially allows VATS manipulation with one less intercostal access site.

We believe that the role of lasers in thoracoscopic operations is underappreciated by most surgeons. Surgical lasers can function as a primary or adjunctive tool for resection and coagulation in many thoracoscopic procedures, but experience with this technology must be acquired [8, 10, 12–14]. We emphasize the importance of developing an appreciation for the various laser wavelength–pulmonary tissue interactions that occur. The thoracic surgeon must also have an understanding of basic laser safety practices before using lasers in the setting of thoracoscopy [15, 16].

A potential problem encountered with VATS procedures involves the removal of pathological tissues from the thoracic cavity. On occasion, we have simply expanded one of the intercostal access incisions to 3 to 4 cm (without spreading the ribs) to allow extraction of the specimen. Under most circumstances, an expanded incision is not necessary, and the specimen can be extracted by placing it in a sterile glove or a commercially available plastic sleeved device (Pleatman sac; Cabot Medical, Langhorne, PA) introduced into the thoracic cavity through one of the intercostal access sites.

Suggested Approaches to Various Thoracic Surgical Problems

Wedge Resection of Peripheral Pulmonary Nodules and Closed Lung Biopsy

The present VATS approaches are appealing for the evaluation of diffuse infiltrative lung disease and for the surgical excision of the indeterminate pulmonary nodule (see Table 1). Wedge resection of pulmonary tissue equivalent to that achieved through open thoracotomy is obtainable with VATS techniques [8–10, 17]. We [17] have now established a standard intercostal access strategy for wedge resection biopsy of diffuse infiltrative disease. A more flexible approach must be taken for VATS resection of the indeterminate pulmonary nodule (Fig 4). We emphasize the importance of careful examination of the preoperative computed tomographic scan of the chest before planning of the intercostal access strategy for VATS pulmonary nodular resection [8–11].

In general, we initiate a closed lung biopsy procedure by introducing the thoracoscope through a trocar-protected site at the sixth or seventh ICS in the midaxillary to posterior axillary line. After thoracoscopic exploration, a second access site is chosen in the fifth ICS along the anterior axillary line. We routinely choose these two initial sites for VATS access along the fifth to seventh ICS to obtain instrument positioning along the interlobar fissures. This alignment facilitates exposure and manipulation of most areas of lobar pathology and also allows the

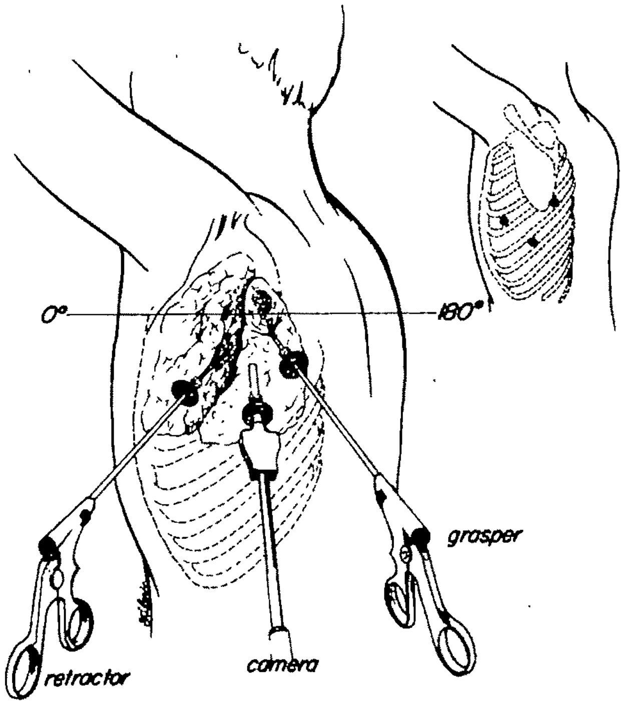


Fig 4. Typical positioning of the thoracoscopic instruments and thoracoscopic camera for an approach to a lesion in the superior segment of the left lower lobe of the lung.

application of the endoscopic stapler along a variety of parenchymal edges of the lung for potential wedge resection of infiltrative lung disease. The endoscopic stapler should be introduced into the chest through a trocar-protected ICS access site at a distance from the target lesion so that the jaw mechanism of the stapler can be fully opened and freely maneuvered about the target pathology.

Use of the "operating" thoracoscope frequently allows us to accomplish wedge resection with only two sites of ICS access. A reusable forceps 5 mm in diameter (45 cm in length) is introduced through the operative channel of the thoracoscope to grasp an appropriate site along the edge of the lung. The endoscopic stapler (United States Surgical Corp, Norwalk, CT) is then introduced through the anterior fifth ICS and positioned on the pulmonary tissue to begin the V wedge resection. We then reverse the position of the thoracoscope and forceps to the anterior fifth ICS site to complete the V wedge resection from the opposite side of the pathologic tissue with the endoscopic stapler introduced through the other ICS access site. Alternatively, we can create a third ICS access site through the posterior seventh to ninth ICS to position the thoracoscopic camera and directly view the endoscopic stapler and grasping forceps being used for wedge resection through the fifth or sixth ICS site [17].

Video-assisted thoracic surgical lobectomy is also a reality. We emphasize that this is an area of investigation that we would *not* recommend to the occasional or inexperienced thoracoscopic surgeon. Furthermore, objective analyses of the differential morbidity, cost, and therapeutic effectiveness of VATS lobectomy versus open lobar resection will be required before the VATS approach can be considered a viable treatment option for most patients. We remain cautiously intrigued with the VATS approach for lobar resection in carefully selected patients. Although the number of patients on whom we have performed VATS lobectomy is limited, our preliminary experience has been gratifying (see Table 1). A small "utility" thoracotomy 6 to 10 cm in length is needed (without spreading the ribs) to introduce endoscopic (or standard) instruments during the course of the dissection and ultimately to extract the pulmonary lobar tissue.

Apical Bullous Disease

Other investigators [13, 18] have described novel techniques of laser ablation and endoscopic ligation of the apical bullae responsible for spontaneous pneumothoraces. We [19], however, advocate VATS stapled resection of bullous disease, a procedure technically equivalent to current open thoracotomy approaches (see Table 1). Proper intercostal placement of instruments and thoracoscope is critical for an expeditious and accurate VATS exploration and stapled resection of apical bullous disease. We commonly position the thoracoscopic camera through the sixth ICS along the midaxillary line (Fig 5). The endoscopic stapler is introduced through the posterolateral fourth or fifth ICS in the area of the auscultatory triangle. A grasping instrument is placed through a small stab wound at the lateral border of the pectoralis muscle in the fourth ICS. This instrument and camera positioning allows expeditious resection of bullous disease along the

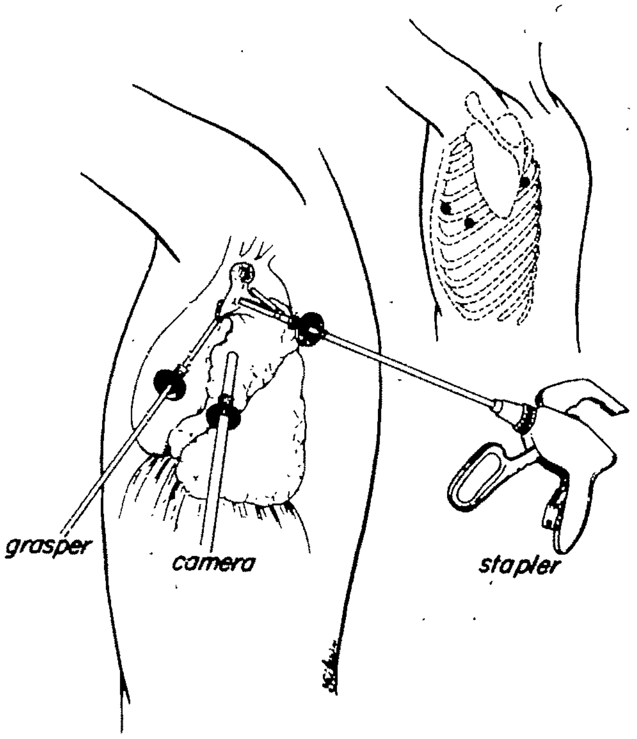


Fig 5. Thoracoscopic approach to apical bullous disease in the left upper lobe.

apex of the upper lobe and the superior segment of the lower lobe. A mechanical pleurodesis or apical pleurectomy can be performed after the stapled bullectomy using these ICS access sites without difficulty.

Approach to Aortopulmonary Window, Subazygos Nodes, or Midesophagus

Thoracoscopic exploration of the thoracic cavity to identify potential metastatic pleural involvement is an accepted diagnostic maneuver for select patients with thoracic malignancy [2, 3, 5]. We have also found the VATS approach to be a valuable adjunct to cervical mediastinoscopy for the staging of suspected malignant spread to lower mediastinal lymph nodes (Fig 6). We have generally abandoned the Chamberlain [20] anterior mediastinotomy procedure in favor of the VATS approach to assess the aortopulmonary window and subazygos lymph node regions (see Table 1). The dissection and sampling of lymph nodes and other pathologic processes in these locations have been safe, accurate, and technically feasible. The thoracoscope is usually introduced through the fifth or sixth ICS along the posterior axillary line. Second and third ICS access sites are obtained through the fifth ICS in the auscultatory triangle and along the anterior axillary line at the fourth ICS for dissecting instruments and the endoscopic clip applier. A final access site through the seventh ICS is usually chosen in the midaxillary line to introduce a lung-retracting instrument to improve the viewing of these nodal regions. A nodal dissection with visibility superior to that obtained through the anterior mediastinotomy approach is consistently achieved.

We also prefer this VATS approach over anterior mediastinotomy to obtain tissue for the diagnosis of mediastinal and hilar masses of suspected lymphomatous or other causes [21]. The less extensive and laterally located VATS incisions can avoid potential delays in appropriate medical treatment (radiation therapy or chemotherapy) related to healing of the anterior mediastinotomy chest wound. We also find the small intercostal access incisions of the VATS approach cosmetically superior to the anterior mediastinotomy wound.

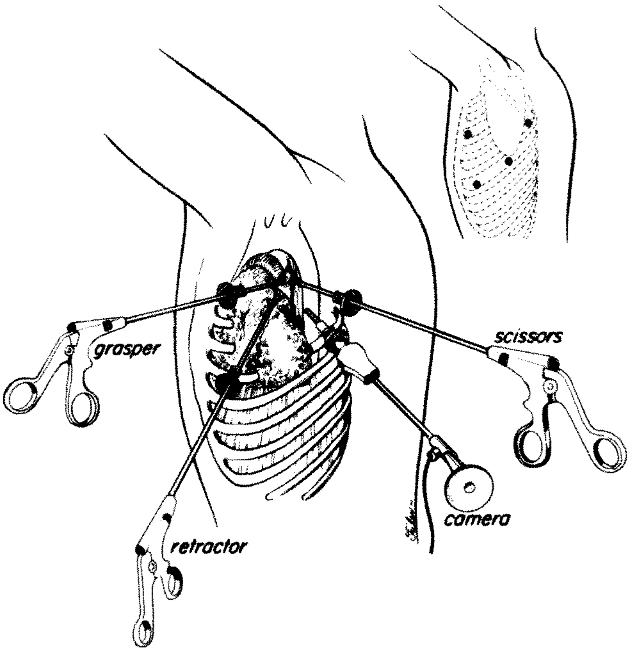


Fig 6. Thoracoscopic approach to the aortopulmonary (A/P) window or subazygos and subcarinal lymph node groups on the right.

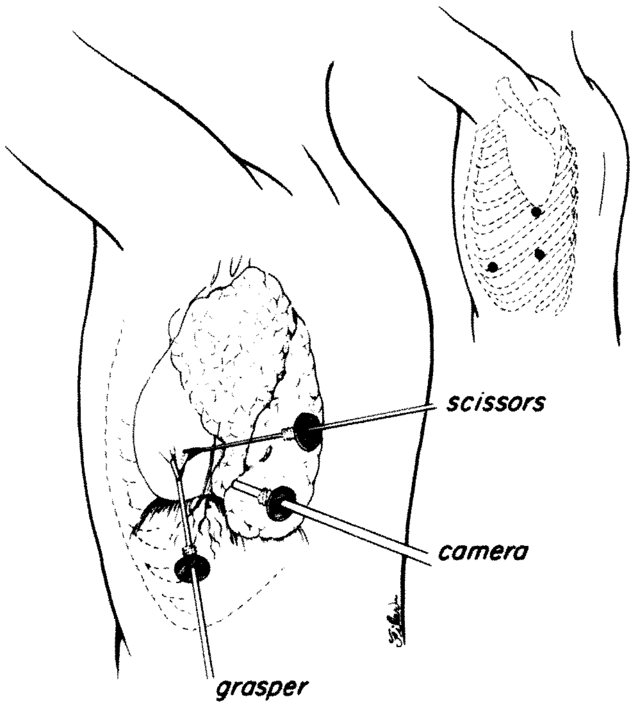


Fig 7. Left-sided thoracoscopic approach for pericardiectomy.

Pericardiectomy

Pericardiectomy is another useful application of thoracoscopic surgery (see Table 1). We use a left-sided thoracoscopic approach, if all other conditions are equal, as the extent of resection achievable is greater through the left pleural space (Fig 7). If a previous left thoracotomy has been performed or if a large right-sided pleural effusion is present, we use the right-sided approach. We now prefer VATS pericardiectomy over the subxiphoid pericardial window technique for many patients, as the VATS approach also offers the potential to diagnose and manage any associated pleural pathology, and as we find that a VATS pericardial resection equivalent to open thoracotomy can be achieved in most instances [22, 23].

The placement of the thoracoscope and instruments is usually selected to approach the pericardium from slightly posterior and lateral fifth, seventh, and ninth ICS positions. We emphasize the importance of using a somewhat posterolateral approach to VATS pericardial resection to improve visibility of the entire operative field and enhance maneuverability of the endoscopic instruments. The endoscopic GIA stapler (United States Surgical Corp) has been used to facilitate pericardiectomy, but we rely

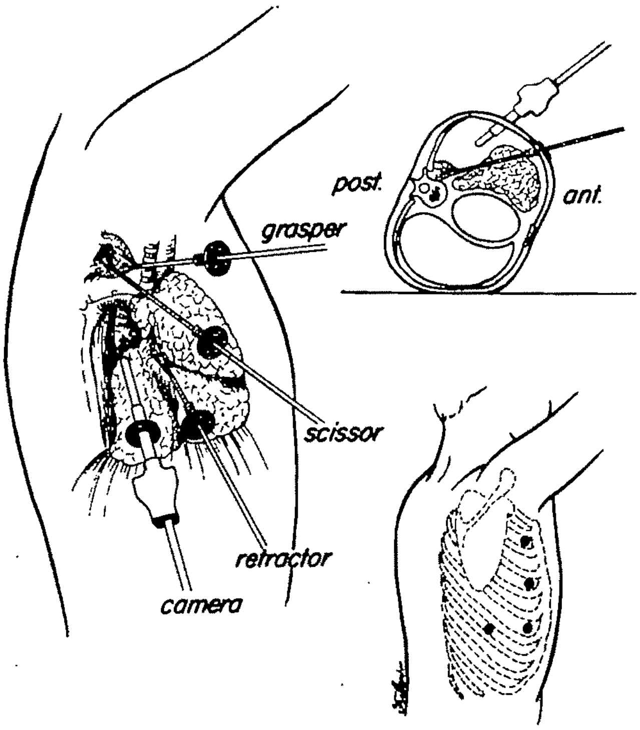


Fig 8. Right thoracoscopic approach to posterior neurogenic tumors and dorsal sympathectomy.

primarily on direct endoscopic scissor resection. We think the visibility of the distal extent of the pericardium to be resected superior with a direct scissor-resection technique. The electrocautery should be used cautiously in this technique because of the potential for ventricular fibrillation. The surgical team should have sterile external defibrillation equipment on the operative field for electroconversion should manipulation cause a ventricular fibrillatory event.

Additional caution during dissection about the phrenic nerve is important as it progresses cephalad toward the pulmonary hilum. Injury to the phrenic nerve (and the left atrial appendage) can occur if care is not taken. We usually resect an 8-cm square piece of pericardium anterior to the phrenic nerve and also attempt resection of a similarly sized segment of pericardium posterior to the phrenic nerve. We stress that adequate postoperative drainage of the pericardial space and any associated pleural effusions remains an important aspect of management of effusive pericarditis [24, 25].

Posterior Mediastinal Masses and Dorsal Sympathectomy

Posterior neurogenic tumors documented to be free of neural canal involvement are ideally suited for VATS resection (see Table 1). Dorsal sympathectomy, when clinically indicated, is also safely and expeditiously approached with VATS techniques [26–28].

As for other intrathoracic pathology, we strategically plan our initial ICS access so as to visualize the lesion from an adequate distance for instrument manipulation. Thus, we usually approach posteriorly located lesions through a slightly anterior ICS access site. Conversely, anterior lesions are approached through slightly posterior axillary ICS sites. We also tilt the operative table to allow gravity assistance for the displacement of the lung (Fig 8).

As most posterior neurogenic tumors are located in the superior costovertebral recess, we will discuss the approach to pathology in this location. The thoracoscope is introduced through the fifth ICS at the midaxillary line, and a lung retractor is placed through the fourth or sixth ICS in the anterior axillary line. Endoscopic dissectors/graspers and a clip applier are introduced through ICS access at the second ICS. An endoscopic scissors is usually introduced through the midaxillary to anterior axillary line at the third to fourth ICS, although we occasionally use a sixth to seventh midaxillary to posterior axillary ICS location. This approach has allowed a safe and complete resection of several benign posterior neurogenic tumors and successful dorsal sympathectomy in all instances.

Anterior Mediastinal Masses

We [29] have used the VATS approach for the biopsy and the resection of several anterior mediastinal masses (see Table 1). Most recently, we have also used this approach to accomplish total thymectomy in the management of myasthenia gravis and to resect aberrant intrathoracic parathyroid adenomatous tissue.

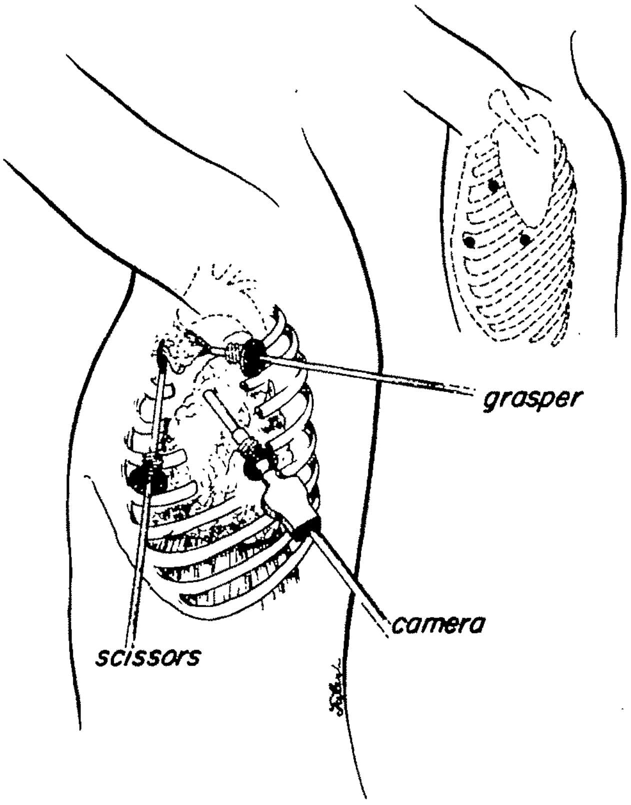


Fig 9. Left thoracoscopic approach to anterior mediastinal masses and thymectomy.

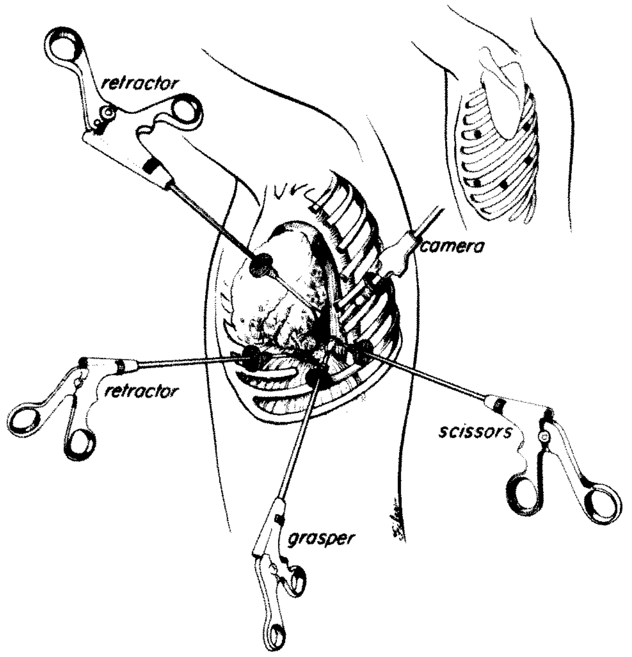


Fig 10. Right thoracoscopic approach to the distal esophagus for esophagomyotomy.

We usually position the thoracoscope through the fifth ICS in the midaxillary to posterior axillary line (Fig 9). Grasping instruments are introduced through a small stab wound in the second or third ICS in the midaxillary line, and endoscopic scissors are usually introduced in a similar fashion through the fifth or sixth ICS in the anterior axillary line. A fourth site of instrument access is often established through the seventh ICS in the midaxillary to anterior axillary line to provide alternate positioning of scissors and graspers or to provide retraction of the lung during the course of the dissection.

Distal Esophageal Lesions

The VATS approach to the distal esophagus for transthoracic truncal vagotomy or esophagomyotomy for the management of achalasia usually requires positioning of the thoracoscope through the seventh ICS in the midaxillary to posterior axillary line (Fig 10). The thoracoscope is directed toward the patient's esophageal hiatus, and accessory ICS access sites are established at the fourth ICS in the anterior axillary line (lung retraction), the seventh ICS in the anterior axillary line (diaphragmatic retraction), and the sixth and eighth ICSs along the posterior axillary line for grasping forceps and endoscopic scissors. A flexible gastroscope can be used to stent the esophagus and to transilluminate and insufflate the lumen of the esophagus to ensure mucosal integrity during the course of the dissection. We, however, prefer to simply introduce a 40F to 48F Maloney esophageal bougie into the esophagus through the mouth to assist in identifying the esophagus and the plane of submucosal dissection. It is often helpful to position the television monitor or monitors toward the foot of the operating table to assist the operators with their orientation during the procedure.

Dissection and mobilization of the distal esophagus and VATS esophagomyotomy technically similar to open techniques can be precisely performed. Thoracoscopic magnification facilitates the accuracy with which this technique can be performed and also helps identify the distal extent of the esophagomyotomy required. Care is taken to avoid an overzealous dissection at the gastroesophageal junction to avoid injury to the anatomical structures preventing gastroesophageal reflux. A concomitant antireflux procedure is not performed.

We emphasize that VATS esophagomyotomy remains a highly investigative procedure at this time. The surgical standard for esophagomyotomy remains open transthoracic myotomy with or without partial fundoplication.

Comment

Video-assisted thoracic surgery appears to offer the potential benefit of reduced morbidity for patients with a number of thoracic surgical problems. This potential can be diminished if extended operative time and imprecise handling of the intrathoracic tissues result from improper (or poorly designed) surgical approaches to the target pathology. The potential disadvantages and concerns include instrumentation, vascular control, pleural seeding, incomplete staging, the learning curve, and overextension of indications. The VATS learning curve can be steep, slow, and discouraging if repeated difficulties with endoscopic instruments and camera positioning limit the dexterity of the thoracic surgical team. It is our hope that difficulties with the basic conduct of VATS operations and with the proper (strategic) intercostal positioning of thoracoscopic instrumentation can be minimized through the information provided in this report.

References

1. Jacobaeus HC. The practical importance of thoracoscopy in surgery of the chest. Surg Gynecol Obstet 1922;34:289–96.
2. Miller JI, Hatcher CR Jr. Thoracoscopy: a useful tool in the diagnosis of thoracic disease. Ann Thorac Surg 1978;26: 68–72.
3. Thomas P. Thoracoscopy: an old procedure revisited. In: Kittle CF, ed. Current controversies in thoracic surgery. Philadelphia: W.B. Saunders, 1986:101–12.
4. Brandt H, Loddenkemper R, Mai J. Atlas of diagnostic thoracoscopy. Indications-techniques. New York: Thieme Medical, 1985:1–46.
5. Page RD, Jeffrey RR, Donnelly RJ. Thoracoscopy: a review of 121 consecutive surgical procedures. Ann Thorac Surg 1989; 48:66–8.
6. Oakes DD, Sherck JP, Brodsky JB, Mark JBD. Therapeutic thoracoscopy. J Thorac Cardiovasc Surg 1984;87:269–73.
7. Benumof JL. Physiology of the open chest and one-lung ventilation. In: Kaplan JA, ed. Thoracic anesthesia. New York: Churchill Livingstone, 1983:287–316.
8. Landreneau RJ, Herlan DB, Johnson JA, Boley TM, Nawarawong W, Ferson PF. Thoracoscopic neodymium:yttrium-aluminum garnet laser–assisted pulmonary resection. Ann Thorac Surg 1991;52:1176–8.
9. Mack MJ, Aronoff RJ, Acuff TE, Douthit MB, Bowman RT, Ryan WH. Present role of thoracoscopy in the diagnosis and treatment of diseases of the chest. Ann Thorac Surg 1992;54: 403–9.

10. Landreneau RJ, Hazelrigg SR, Ferson PF, et al. Thoracoscopic resection of 85 pulmonary lesions. Ann Thorac Surg 1992;54:415–20.
11. Daly BDT, Faling LJ, Diehl JT, Bankoff MS, Gale ME. Computed tomography–guided minithoracotomy for the resection of small peripheral pulmonary nodules. Ann Thorac Surg 1991;51:465–9.
12. LoCicero J III, Frederiksen JW, Hartz RS, Kaufman MW, Michaelis LL. Experimental air leak in lung sealed by low-energy carbon dioxide laser irradiation. Chest 1985;87:820–2.
13. Rusch VW, Schmidt R, Shoji Y, Fujimura Y. Use of the argon beam electrocoagulator for performing pulmonary wedge resections. Ann Thorac Surg 1990;49:287–91.
14. Torre M, Belloni P. Nd:YAG laser pleurodesis through thoracoscopy: new curative therapy in spontaneous pneumothorax. Ann Thorac Surg 1989;47:887–9.
15. LoCicero J III, Frederiksen JW, Hartz RS, Michaelis LL. Laser-assisted parenchymal-sparing pulmonary resection. J Thorac Cardiovasc Surg 1989;97:732–6.
16. Landreneau RJ, Hazelrigg SR, Johnson JA, Boley TM, Nawarawong W, Curtis JJ. Neodymium:yttrium-aluminum garnet laser–assisted pulmonary resections. Ann Thorac Surg 1991;51:973–8.
17. Ferson PF, Landreneau RJ, Dowling RD, et al. Thoracoscopic vs. "open" lung biopsy for the diagnosis of infiltrate lung disease. J Thorac Cardiovasc Surg (in press).
18. Nathanson LK, Shimi SM, Wood RAB, Cuschieri A. Videothoracoscopic ligation of bulla and pleurectomy for spontaneous pneumothorax. Ann Thorac Surg 1991;52:316–9.
19. Hazelrigg SR, Landreneau RJ, Mack MJ, et al. Thoracoscopic stapled resection for spontaneous pneumothorax. J Thorac Cardiovasc Surg (in press).
20. McNeill TM, Chamberlain JM. Diagnostic anterior mediastinotomy. Ann Thorac Surg 1966;2:532–9.
21. Lewis RJ, Caccavale RJ, Sisler GE. Imaged thoracoscopic surgery: a new thoracic technique for resection of mediastinal cysts. Ann Thorac Surg 1992;53:318–20.
22. Miller JI, Mansour KA, Hatcher CR Jr. Pericardiectomy: current indications, concepts, and results in a university center. Ann Thorac Surg 1982;34:40–5.
23. Piehler JM, Pluth JR, Schaff HV, Danielson GK, Orszulak TA, Puga FJ. Surgical management of effusive pericardial disease. J Thorac Cardiovasc Surg 1985;90:506–16.
24. Little AG, Kremser PC, Wade JL, Levett JM, DeMeester TR, Skinner DB. Operation for diagnosis and treatment of pericardial effusions. Surgery 1984;96:738–44.
25. Naunheim KS, Kesler KA, Fiore AC, et al. Pericardial drainage: subxiphoid vs. transthoracic approach. Eur J Cardiothorac Surg 1991;5:99–104.
26. Landreneau RJ, Dowling RD, Ferson PF. Thoracoscopic resection of a posterior mediastinal mass. Chest (in press).
27. Rodgers BM, Ryckman FC, Moazam F, Talbert JL. Thoracoscopy for intrathoracic tumors. Ann Thorac Surg 1981;31:414–20.
28. Kux M. Thoracic endoscopic sympathectomy in palmar and axillary hyperhidrosis. Arch Surg 1978;113:264–6.
29. Landreneau RJ, Dowling RD, Castillo WM, Ferson PF. Thoracoscopic resection of an anterior mediastinal tumor. Ann Thorac Surg 1992;54:142–4.

The acquisition of new knowledge in thoracic surgery is a continuum. Ideas and practices may change significantly as a result of experience, but there have been limited ways to communicate easily the reasons for such modifications.

The purpose of this section is to present brief follow-up reports from authors whose work was previously published in The Annals of Thoracic Surgery. *The goal is to learn whether the original conclusions have stood the test of time, and whether or not previously recommended techniques have been modified, replaced, or discarded. Contributions to* Update *are short progress reports that do not preclude subsequent, more complete articles.*

Thomas B. Ferguson, MD, Editor
John R. Benfield, MD, Associate Editor

1985: Chemoradiation Therapy and Resection for Carcinoma of the Esophagus: Short-term Results

Edward F. Parker, M.D., Richard D. Marks, Jr., M.D., John M. Kratz, M.D.,
Amer Chaikhouni, M.D., E. Taliaferro Warren, M.D.,
and David M. Bartles, M.S.

ABSTRACT The purpose of this report is to record the results of a treatment protocol for patients with carcinoma of the esophagus. In May, 1980, we initiated a program of chemoradiation therapy preliminary to resection in patients in whom the protocol was applicable. The chemotherapy consisted of mitomycin-C, 10 mg as a bolus intravenous injection on day 1, and 5-fluorouracil, 1,000 mg per square meter of body surface area in 1,000 ml of 5% glucose solution in distilled water given intravenously on each of days 1 through 4. The radiation therapy consisted of 3,000 rads in three weeks using cobalt 60 or 6 MeV or greater, with ports to cover the tumor and mediastinum. This protocol was given to patients with primary carcinoma of the esophagus whose disease remained or became operable during or following the course of the chemoradiation.

Among the patients treated according to the protocol, the operability rate was increased. The resectability rate remained about the same as in our previous experience. The operative mortality was lessened appreciably. The percentage of resected specimens of the esophagus showing residual tumor decreased. However, the absence of any residual tumor in the surgical specimen has not conferred any improved chance of long-term survival to date. There has been a two-year survival of 33% (7/21) among the small group having chemoradiation therapy prior to resection, and this figure is roughly the same as that in our previously reported series of patients treated by preoperative irradiation (4,500 rads in three weeks) and resection without the chemotherapeutic adjunct. The observations are short term, but 12 of 31 patients (39%) having chemoradiation therapy followed by resection are still alive. This may be an encouraging portent.

1992 Update: Edward F. Parker, MD

Division of Cardiothoracic Surgery, Department of Surgery, Medical University of South Carolina,
Charleston, South Carolina

The purpose of the program was to observe the effect of concomitant preoperative chemotherapy consisting of mitomycin-C and 5-fluorouracil and radiation therapy in the treatment of 129 patients with primary squamous cell carcinoma of the esophagus seen between May 1980 through April 1984.

Only 33 patients were able to complete the protocol. Observations were continued so that each patient was observed through 1989 and had a minimum period of observation of 5 years, unless death occurred sooner. The operative mortality was 12% (4/33). There was no viable residual tumor in the surgical specimen of the esophagus in 33% (11/33) of those patients completing the triple therapy. However, in 2 of the 11 patients metastases were found in left gastric lymph nodes, and in 1 of the 11, there was a minute esophageal perforation, without complications. The 2-year survival rate was 33% (11/33) and the 5-year survival rate was 15.5% (5/33). Among the 11 patients having 2-year survival, the surgical specimen was normal in 6 and abnormal in 5. Of the 5 patients having 5-year survival, the surgical specimen was normal in 3 and abnormal in 2. The absence of tumor in the surgical specimen did not appear to confirm any better chance for long-term survival. These data were compared with our 1967 to 1975 series of 75 patients receiving only preoperative irradiation and resection. There was no significant difference in the survival rates at 2 years (20% in the 1975 group versus 33% in the current group; $p = 0.2118$) or at 5 years (10% in the 1975 group versus 15.4% in the 1984 group; $p = 0.5796$).

The results of ongoing additional clinical trials are not ready for submission for publication in view of the short period of observation since the institution of therapy.

References

1. Parker EF, Marks RD Jr, Kratz JM, et al. Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results. Ann Thorac Surg 1985;40:121–5.
2. Parker EF, Reed CE, Marks RD Jr, et al. Chemotherapy, radiation therapy, and resection for carcinoma of the esophagus: long term results. J Thorac Cardiovasc Surg 1989;98:1037–44.

Address reprint requests to Dr Parker, Division of Cardiothoracic Surgery, Department of Surgery, Medical University of South Carolina, 171 Ashley Ave, Charleston, SC 29425-2279.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:808 • 0003-4975/92/$5.00

CORRESPONDENCE

Esophageal Perforation

To the Editor:

I read with interest the excellent review entitled "Esophageal perforation: a continuing challenge," by W. G. Jones II and Robert J. Ginsberg, published in *The Annals of Thoracic Surgery* [1]. Dr Jones and Dr Ginsberg quoted our article [2] as having 61 cases of esophageal perforations with an overall mortality of 30%. We have reported 64 cases of esophageal perforations, including 2 cases that were treated nonoperatively because the perforations were contained: one was a cervical perforation due to a foreign body, and the other was diagnosed immediately after a rigid esophagoscopy with biopsy of a peptic stricture. Both patients survived. An additional patient had an abdominal perforation that was closed primarily, but was excluded from Table 3 because the latter compared cervical versus thoracic operations. The third patient also survived. The overall mortality was 28% (18/64). Although this is a small difference from that reported in Dr Jones and Dr Ginsberg's review, nevertheless it is important.

Safuh Attar, MD

Division of Thoracic and Cardiovascular Surgery
University of Maryland Hospital
22 S Greene St
Baltimore, MD 21201

References

1. Jones WG II, Ginsberg RJ. Esophageal perforation: a continuing challenge. Ann Thorac Surg 1992;53:534–43.
2. Attar S, Hankins JR, Suter CM, et al. Esophageal perforation: a therapeutic challenge. Ann Thorac Surg 1990;50:45–9.

Reply

To the Editor:

We thank Dr Attar for his letter regarding our review on esophageal perforation. In our review of the article by Attar and associates, the 3 additional cases that Dr Attar mentioned were indeed not included in the preparation of data for Table 1. Thus, as he has stated, the tabulated mortality should indeed be 18/64 (28%) rather than the 18/61 (30%) that we quoted. We apologize to Dr Attar and his associates for this error and appreciate his efforts in its correction.

William G. Jones II, MD
Robert J. Ginsberg, MD

The New York Hospital-Cornell Medical Center
525 E 68th St
New York, NY 10021

Ross' First Homograft Replacement of the Aortic Valve

To the Editor:

I read with interest the article by Hopkins and associates [1]. Their report took me back 30+ years when I was working on the aortic homograft and the heterologous aortic valve. At that time I was unaware of the experimental work of Gross, Lam [2], and Heimbecker. It was Murray's [3] successful clinical use of placing the homograft in the descending aorta that prompted me to devise the method of placing the aortic valve in the "subcoronary position" [4]. Once I realized this was a feasible clinical proposition, I phoned Donald Ross at Guy's Hospital and described the method to him. He expressed considerable interest and mentioned it to Lord Brock—his chief at that time—who also considered it possible. During the same conversation I asked Ross—who was doing far more open heart valve operations than I was—to let me know if and when he proposed inserting a freeze-dried homologous aortic valve into the "subcoronary position." As reported by Hopkins and associates [1], Ross had started collecting a bank of freeze-dried valves and luckily, as it subsequently turned out, he was forced to insert a valve in the orthotopic position with a successful outcome [5]. He kindly phoned me after the operation and apologized for not letting me know before the operation, as his hand had been forced!

However, Ross was not the first to place an autologous aortic valve in the orthotopic position. This was first achieved by Bill Bigelow and Raymond Heimbecker in 1961 (Bigelow W, Heimbecker R, personal communication, 1987). The patient, sadly, died of an infarct after 24 hours. For the record and history of cardiac surgery, they therefore were the first to insert an aortic homograft in the subcoronary position.

Truly, originality is only original when you are the first!

Alfred J. Gunning, FRCS

Department of Cardio/Thoracic Surgery
Medical University of South Africa
PO Box 124
Medunsa 0204
South Africa

References

1. Hopkins RA, St. Louis J, Corcoran C. Ross' first homograft replacement of the aortic valve. Ann Thorac Surg 1991;52:1190–3.
2. Lam CR, Acam HH, Mennell ER. An experimental study of aortic valve homografts. Surg Gynecol Obstet 1952;94:129–35.
3. Murray G. Homologous aortic valve segment transplants as surgical treatment for aortic and mitral insufficiency. Angiology 1956;7:466–71.
4. Duran CG, Gunning AJ. A method for placing a total homologous valve in the "subcoronary position." Lancet 1962;2:779–89.
5. Ross DN. Homograft replacement of the aortic valve. Lancet 1962;2:487.

Reply

To the Editor:

My colleagues and I have read with great interest the letter by Mr Gunning concerning the contribution by Drs Bigelow and Heimbecker. I agree that history is best served by such accuracy, and certainly it appears that these individuals deserve the credit for the first placement of the homologous aortic valve in the orthotopic position in a human. Mr Gunning's clarification is all the more important because as far as I am aware, there is no other record in the international literature of this case. Because their patient died, I believe that Mr Ross deserves credit for the first *successful* placement of a homograft aortic valve in the orthotopic position in a human. I am intrigued that it was Mr Gunning's experimental work on technique that was generously shared with Mr Ross that allowed the successful clinical insertion. Mr Ross himself admitted that he had not performed such a procedure in an animal. This to me is a most significant aspect of this historical vignette. It underscores the importance of the informal network that those of us involved in reconstructive cardiac

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:809–16 • 0003-4975/92/$5.00

surgery maintain, to speed, simplify, and magnify the exchange of ideas, methods, and techniques.

Richard A. Hopkins, MD

Department of Surgery
Georgetown University Medical Center
3800 Reservoir Road NW
Washington, DC 20007-2197

Reply

To the Editor:

I am grateful to Mr Gunning for researching the history of the aortic homograft so thoroughly. I have no doubt that in every field of endeavour there will be prior claims registered or uncovered as far back probably as Leonardo da Vinci. I must confess that I was not aware of Heimbecker and Bigelow's attempt, but knowing these two pioneers, I am not surprised. We like to credit Conrad Lam with the concept of using the homograft aortic valve, which he published in 1952. It was his work that stimulated us and we followed it up in the dog laboratory in Guy's Hospital under the auspices of Lord Brock (Brewin) [1]. The rest is history.

Donald Ross, FRCS

25 Upper Wimpole St
London W1M 7TA
England

Reference

1. Brewin EG. The use of tissue transplants in the surgery of cardiac valve disease—an experimental study. Guy's Hosp Rep 1956;105:328–39.

Continuous Normothermic Blood Cardioplegia: Simplified Delivery Circuit

To the Editor:

We have been following with keen interest the development of "warm" blood cardioplegia [1–3]. We have used this method of myocardial protection in 50 patients. Patients with congenital heart disease formed a predominant group in our experience, besides those with coronary and valvular procedures. In the first 25 patients we used the pump circuit and dilution of blood as reported by Lichtenstein and associates. However, in the last 25 patients we have adopted the following modifications in the method of cardioplegia delivery which, we believe, have simplified the pump circuit considerably: (1) use of blood directly from oxygenator for continuous perfusion of aortic root, (2) fixed flow rate of aortic root perfusion (1 to 2 mL · kg^{-1} · min^{-1} to maintain aortic root pressure at 80 mm Hg) and varying potassium concentration for induction and maintenance of cardiac arrest, and (3) use of a syringe pump for infusing potassium chloride solution into the cardioplegia line just beyond the cardioplegia delivery pump (Fig 1).

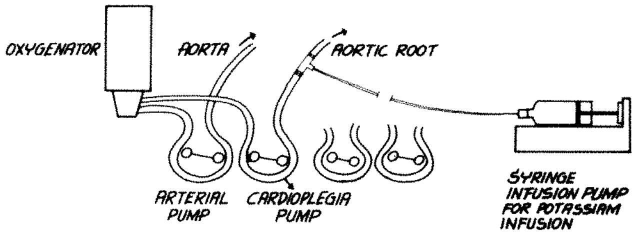


Fig 1. Simple delivery circuit for continuous normothermic blood cardioplegia.

The syringe infusion pump is filled with the commercially available potassium chloride solution, and it is connected to the side port of the straight connector interposed in the cardioplegia line just beyond the cardioplegia pump. Once full flows are achieved on standard cardiopulmonary bypass the aorta is clamped and the syringe pump is switched on at a predetermined setting to deliver a 0.1 mEq · kg^{-1} · min^{-1} dose of potassium chloride solution to stop the heart in 3 to 5 minutes (induction dose), and then the infusion rate is adjusted to give 0.005 to 0.01 mEq · kg^{-1} · min^{-1} potassium to sustain the cardiac arrest (maintenance dose). Small purges may be needed occasionally to sustain the arrest. In the final stages of intracardiac repair the potassium infusion is stopped but continuous normothermic infusion is continued for some time, and the aorta is declamped with suction on the aortic root.

In our practice, we believe that this is a much simpler circuit to handle and it allows more precise control over the amount of potassium that is being delivered. Because we are using blood directly from the oxygenator, there is no need for any further heat exchanger in the circuit. The use of additional crystalloid solution for dilution and the use of solutions containing varying quantities of potassium are also avoided [1, 3, 4].

Ponangi V. Satyanarayana, MS, MCh
Podila Sita Rama Rao, MS, MCh
Kesavaram Madhusudhana Rao, BSc, CCP
Alluru Sarath Chandra, MS
Kanchumarthi Sudhakar Rao, MS
Karri Venkat Reddy, MS

Department of Cardio Thoracic Surgery
Nizam's Institute of Medical Sciences
Hyderabad, 500 482
India

References

1. Lichtenstein SV, Ashe KA, El Dalati H, Cusimano RJ, Panos A, Slutsky AS. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
2. Lichtenstein SV, Fremes SE, Abel JG, Christakis GT, Salerno TA. Technical aspects of warm heart surgery. J Card Surg 1991;6:2:278–84.
3. Lichtenstein SV, El Dalati H, Panos A, Slutsky AS. Long cross-clamp with warm heart surgery. Lancet 1989;1:1443.
4. Tutassaura H. Continuous warm blood cardioplegia. Ann Thorac Surg 1991;51:866.

Thromboelastogram and Postoperative Hemorrhage

To the Editor:

The recent article "Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients" by Wang and associates [1] provides an interesting contrast to most prior work in this area [2–5]. Indeed, this represents the only report that finds no predictive accuracy or advantage of thromboelastography (TEG) over routine coagulation testing. Perhaps some of the following discussion and points may explain this obvious discrepancy.

Wang and associates note the most common abnormalities before cardiopulmonary bypass were hypocoagulability and fibrinolysis. The mean values for TEG reaction time values were considerably higher than postbypass values, and the mean activated clotting time values were higher (156 ± 28.5 seconds) than values routinely considered as normal. These two facts suggest that some patients must have been receiving preoperative heparin infusions.

Low-dose preoperative heparin infusions may cause profound prolongations of the reaction time value and also affect the coagulation time and maximum amplitude. The reaction time value may be of infinite length with such therapy, and if this occurred in any of the 101 patients studied, then correlations between activated clotting time, activated partial thromboplastin time, and the TEG reaction time value would be largely dependent on how the statistical analysis of these data was handled.

The demographics given do not allow one to decide if that was actually a problem for the investigators. Other pertinent pieces of information such as the incidence of emergency cases and use of platelet inhibitors and fibrinolytics are missing. The preoperative data show a tendency toward fibrinolysis (mean amplitude 60 minutes after the maximum amplitude was 20% less than the maximum amplitude). This alone suggests that some patients must have received streptokinase tissue plasminogen activators or urokinase therapy before entrance into the operating rooms. The large standard deviation in the amplitude 60 minutes after the maximum amplitude also suggests that some subpopulation of patients (n = 16) had profound lysis.

If patients on thrombolytic therapy and heparin therapy are included in the study population, it would be unlikely that the maximum amplitude would have any correlation with platelet count, as both of these therapies greatly affect platelet function. The TEG tests not only platelet count, but also platelet function. Our prior studies wherein some weak correlations were demonstrated before bypass avoided patients with heparin or thrombolytic therapy specifically to avoid these compounding variables [3].

After bypass the only coagulation data collected were from the time immediately after protamine administration. Those coagulation data were correlated with measured chest tube drainage for periods over the subsequent 24 hours. Once again, a great deal of pertinent information is lacking. There is no report of the mean, median, and standard deviations for chest tube blood loss at each measured time interval. All patients were lumped together in the overall correlation data. There are populations of patients that exhibit extremes of hemorrhage, and there is no way of knowing if "severe bleeders" affected the overall correlations.

Conspicuously absent is any discussion of the use of factor and platelet therapy in the immediate postoperative period. In 101 patients it would be nearly impossible to avoid the use of these blood bank products. Once they are administered, the correlation of prior coagulation data (TEG, platelet count) with subsequent chest tube hemorrhage would be negated. Without simultaneous testing and a clearly defined and rigidly followed algorithm for administration, the use of any such blood products seriously damages any conclusions drawn from such correlations.

Patients were reexplored for chest tube bleeding based on surgical criteria—a combination of the speed of blood loss and its hemodynamic consequences. Unfortunately, probably some element of surgical bleeding occurred in the "undefined" population. We will never know what the impact of such blood loss was because these patients were never reexplored. No separate correlations were done between coagulation tests and those patients with abnormal bleeding. Would there have been a difference as compared with the patients with routine chest tube losses?

Data for abnormal coagulation do not agree between Tables 4 and 5. In Table 4, 42 patients have abnormal TEG data after cardiopulmonary bypass, whereas, in Table 5, only 34 are reported to have abnormalities. Why does this discrepancy exist?

No criteria are described for inclusion versus exclusion of patients for the group reported. Were these 101 consecutive patients as a clinical series? The above-described concerns lead to the conclusion that this was performed as exactly that—a clinical series of patients without tight experimental control. As a series, the reported data correspond somewhat with what has been found in one series of more than 500 patients. A surprisingly high incidence of hypercoagulability and fibrinolysis exist. These coagulopathies are heretofore unstudied, and the problem of hypercoagulability is particularly worrisome.

In conclusion, the article by Wang and associates does not prove or disprove the usefulness of TEG monitoring, but it does point out that we have a lot of study remaining regarding coagulation and cardiopulmonary bypass before we understand all the problems.

Bruce D. Spiess, MD

Division of Cardiothoracic Anesthesia
University of Washington School of Medicine
RN-10
Seattle, WA 98195

References

1. Wang J-S, Lin C-Y, Hung W-T, et al. Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients. Ann Thorac Surg 1992;53:435–9.
2. Martin P, Horkay F, Rajah SM, Walker DR. Monitoring of coagulation status using thromboelastography during paediatric open heart surgery. Int J Clin Monit Comput 1991;8: 183–7.
3. Spiess BD, Tuman KJ, McCarthy RJ, DeLaria GA, Schillo R, Ivankovich AD. Thromboelastography as an indicator of post–cardiopulmonary bypass coagulopathies. J Clin Monit 1987;3: 25–30.
4. Tuman KJ, Spiess BD, McCarthy RJ, Ivankovich AD. Comparison of viscoelastic measures of coagulation after cardiopulmonary bypass. Anesth Analg 1989;69:69–75.
5. Whitten C, Allison P, Latson T, Elmore J, Gulden R, Burkhardt D. Thromboelastographic fibrinolysis does not correlate with levels of D-dimers after cardiopulmonary bypass. Anesthesiology 1991;75:A-432.

To the Editor:

In the recent article entitled "Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients" by Wang and associates [1], TEG as well as routine coagulation studies were unable to reliably predict postoperative hemorrhage. Because of the differences in the findings of this study with others examining the predictive effects of TEG after cardiopulmonary bypass [2–4], particular attention should be made to assure the reader that the technical aspects of the coagulation studies performed in this series were similar to those used by other investigators. We are especially concerned about the specific methods used to obtain TEG data because this study uniquely reports a manyfold greater incidence of hypocoagulability before operation in patients undergoing elective cardiac operations compared with previously reported TEG data in this setting.

In our experience, obtaining TEG samples from arterial lines connected to flush devices containing heparin to maintain patency may result in a significant number of samples exhibiting a "factor deficiency"-like tracing when an inadequate volume of blood is withdrawn before obtaining blood for the TEG. In the study by Wang and associates, a larger than expected number of patients (17; 46%) exhibited prebypass TEG tracings consistent with this sampling error, but the authors admittedly did not attempt to determine if these were valid measurements or a result of sampling error. It would be useful to know the sampling technique employed and if it was used consistently throughout the study by all investigators. Perhaps an examination of the activated partial thromboplastin time values that correspond to these samples could help evaluate the presence of methodologic artifact.

Another technical artifact seen with the TEG is the separation of the forming clot from the inner surface of the cuvette resulting in a fibrinolysis-like tracing. This is commonly encountered when there is improper cleaning and contamination of the metal cup and pin components of the thromboelastograph, as well as inadequate precautions to prevent desiccation of blood samples (ie, use of free surface coating with oil). From Wang and associates' descriptions of their methods, we do not know how the metal cuvettes were cleaned between use and are not informed whether samples were performed in duplicate to help identify potential artifactual tracings. We do not have any evidence that the authors attempted to determine if their high incidence of such tracings were real or artifactual. The availability of disposable cup and piston components for the Thromboelastogram Coagulation analyzer (Haemoscope Corp, Morton Grove, IL) may reduce abnormalities encountered from contamination of the reusable metal components.

Wang and associates state that the determination of the accuracy of the TEGs is based on ±20% variation of their data from the normal range; however, they provide no normal range for comparison. If the commonly accepted normal range for the reaction time value of 6 to 12 minutes [3, 5] is used for a point of comparison, then more than 67% of their patients may have exhibited the above-described effect of heparin from an arterial sample during the prebypass period. These findings are also consistent with preoperative heparinization or a warfarin effect. However, Wang and associates do not state if any of the patients in this study were receiving these types of anticoagulants or when they were discontinued. Likewise, no normal ranges are given for the routine coagulation tests performed in the study, so it is difficult to interpret the values that are presented.

Wang and associates also comment that other investigators attribute many prebypass alterations in TEG tracings to the effect of medications that alter platelet function, but they do not present any data on this type of preoperative medications that may have been received by patients in their study. If a great number of these patients were receiving anticoagulation, this could explain the authors' conclusion that factor deficiencies before cardiopulmonary bypass were the most common abnormalities detected by TEG.

Assessment of accuracy is important before the application of any laboratory test. Perhaps the greatest shortcoming of TEG is the lack of standards to aid in evaluating abnormal results. Our vast experience in more than 6,000 consecutive cardiac procedures with the use of TEG as a routine perioperative coagulation monitor has taught us the importance of careful scrutiny of TEG data before arriving at a final interpretation. Although the principles of TEG appear to be simple, successful implementation of this tool for monitoring coagulation in cardiovascular patients requires care and experience in performing the test as well as in interpreting its results. Unless Wang and associates are able to demonstrate that the large number of baseline abnormalities in coagulation were not artifactual, a serious question about methodologic flaws arises and prohibits use of the data presented to support their conclusions. The study does demonstrate that TEG is at least as accurate and probably more accurate than routine coagulation tests even when a high number of unexplainable results are encountered. In addition, this study confirms the specificity of TEG in detecting surgical bleeding in cardiac surgical patients.

Kenneth J. Tuman, MD
Robert J. McCarthy, PharmD
Anthony D. Ivankovich, MD

Department of Anesthesiology
Rush-Presbyterian-St. Luke's Medical Center
1653 W Congress Pkwy
Chicago, IL 60612

References

1. Wang J-S, Lin C-Y, Hung W-T, et al. Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients. Ann Thorac Surg 1992;53:435–9.
2. Spiess BD, Tuman KJ, McCarthy RJ, DeLaria GA, Schillo R, Ivankovich AD. Thromboelastography as an indicator of post-cardiopulmonary bypass coagulopathies. J Clin Monit 1987;3:25–30.
3. Tuman KJ, Spiess BD, McCarthy RJ, Ivankovich AD. Comparison of viscoelastic measures of coagulation after cardiopulmonary bypass. Anesth Analg 1989;69:69–75.
4. Martin P, Horkay F, Rajah SM, Walker DR. Monitoring of coagulation status using thromboelastography during paediatric open heart surgery. Int J Clin Monit Comput 1991;8:183–7.
5. Kang YG, Martin DJ, Marquez J, et al. Intraoperative changes in blood coagulation and thromboelastographic monitoring in liver transplantation. Anesth Analg 1985;64:888–96.

To the Editor:

We read with interest a recent article by Wang and associates [1] entitled "Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients." In agreement with these workers our group [2] also found that in adults TEG failed to predict excessive bleeding postoperatively, and we similarly made the observation of hypercoagulability detected by TEG after cardiopulmonary bypass, albeit at a greater prevalence (60%) than that reported by Wang and associates (13%).

In contrast, in a cohort of pediatric patients undergoing open heart procedures, an abnormal TEG profile in the period immediately after protamine administration was associated with, and was highly predictive of, increased 24-hour postoperative blood loss (sensitivity, 100%; specificity, 73%) [3]. The reason(s) for this apparent anomaly between adults and children remains to be elucidated, but hypercoagulability was not identified in any of the children after operation. Further studies are indicated (in pediatric patients at least) to assess whether TEG is a potentially useful adjunct to conventional coagulation screening, and to establish whether TEG-guided blood product administration conveys advantage over the currently employed empirical approach.

Paul G. Martin, BSc
Ferenc Horkay, MD
Nirmal K. Gupta, MCh
Duncan R. Walker, FRCS

Department of Cardiothoracic Surgery
Killingbeck Hospital
York Rd
Leeds LS14 6UQ
Yorks
United Kingdom

References

1. Wang J-S, Lin C-Y, Hung W-T, et al. Thromboelastogram fails to predict postoperative hemorrhage in cardiac patients. Ann Thorac Surg 1992;53:435–9.

2. Horkay F, Martin P, Gupta NK, Satur CMR, Walker DR. Transient hypercoagulability in adult patients following open heart surgery. Perfusion (in press).
3. Martin P, Horkay F, Rajah SM, Walker DR. Monitoring of coagulation status using thromboelastography during paediatric open heart surgery. Int J Clin Monit Comput 1991;8: 183–7.

Reply

To the Editor:

We appreciate the comments by Drs Spiess and Tuman, who currently are strong advocates of TEG as a tool for monitoring surgical bleeding after cardiopulmonary bypass.

Our findings on TEG contrast greatly with those in their previous publications. However, upon careful examination of the available data, the scientific validity of the TEG, and the TEG techniques employed, we came to the conclusion as to the nonspecific nature of the TEG in providing information on coagulation defects and the difficulty in interpretation of the TEG tracing (ie, differentiating between artifacts and real changes).

Even though TEG technology has existed for more than four decades, there is still a limited understanding of the interactions of various factors (eg, platelet count) and their effects on TEG tracings. In addition, the lack of standards to aid in the evaluation of abnormal TEG results, the long time required for the interpretation of the TEG, and the difficulty of verifying TEG data probably contribute to the lack of popularity of the TEG and its uncertain fate as a reliable clinical technique for monitoring of blood coagulation.

In reaction to our averaged prebypass activated clotting time of 156 seconds, Drs Spiess and Tuman and their associates raised many questions, including whether patients received antithrombolytic therapy or anticoagulation before its determination and whether poor technique was exercised during TEG blood sampling. We appreciate their comments, but we would like to point out that these are also not addressed in their reports [1, 2]. They also did not provide information on normal ranges of the TEG and on preoperative medications [1], or information as to how to guarantee clean instruments and how to identify artifactual tracings.

As to their questions concerning the patient population and patients' condition, our study included only elective scheduled cases; emergency cases and patients receiving antithrombolytic therapy were excluded from the study protocol. We did not study patients who received aspirin, but premedication included persantin given orally. Neither prophylactic blood component therapy nor blood transfusion was given before post–cardiopulmonary bypass blood sampling for the study. Eight patients underwent heparin therapy during and after percutaneous transluminal coronary angioplasty; however, overnight heparin administration was stopped more than 4 hours before operation.

As to the technique of performing the TEG, we are aware of the possibility of contamination with heparin; it is possible that an uncleaned cuvette and piston metal parts may have affected the results obtained. However, there is no absolute way to assure cleanliness or absence of contamination even with disposable cuvettes or with duplicate TEGs run as suggested by Tuman and associates. We strictly followed the procedures and precautions set by the manufacturer and recommended in previous publications.

Our average prebypass activated clotting time value of 156 seconds is similar to the value (157.3 seconds) reported by Drs Spiess and Tuman in their article [1]. Because we used the same technique in both prebypass and postbypass blood sampling, the higher activated clotting time value obtained in the prebypass than in the postbypass period (145 seconds) probably is not related to the blood sampling technique as was suggested by Drs Spiess and Tuman. Regarding the higher prebypass activated clotting time, we are not able to offer any explanation other than what we discussed in our report. The shortened postbypass activated clotting time also might suggest the presence of hypercoagulability.

As to reporting the mean and standard deviation for chest tube blood loss at each measured interval, these values are given in Figure 1 of our report.

We appreciate that Dr Spiess pointed out the mistake in numbers in our Table 4. We would like to make the following corrections: in the "Patients Without Excessive Hemorrhage" column (Thromboelastograms), the correct values are 57 normal and 27 abnormal, instead of 48 normal and 36 abnormal. Accordingly, in the text, page 437, column 1, line 7, "was 41% and 43%, respectively" should be changed to "was 41% and 32%, respectively."

In summary, we carried out our study to determine whether analyzing the TEG of patients after cardiopulmonary bypass would allow us to predict which patients will bleed, and whether the TEG would assist us in rapidly diagnosing and treating the underlying causes of bleeding after cardiopulmonary bypass in a way that routine coagulation tests could not permit. Our results indicate that the TEG fails to predict the likelihood of excessive hemorrhage in patients after cardiopulmonary bypass. The same conclusion has been reported by Martin and associates in their letter and upcoming article. This finding also may explain why the TEG has not gained wide popularity as an important monitoring technique since its development in 1948.

Chung-Yuan Lin, MD
Jian-Sheng Wang, MD

Department of Anesthesia and Critical Care
The University of Chicago
5841 S Maryland Ave, MC4028
Chicago, IL 60637

References

1. Spiess BD, Tuman KJ, McCarthy RJ, DeLaria GA, Schillo R, Ivankovich AD. Thromboelastography as an indicator of post–cardiopulmonary bypass coagulopathies. J Clin Monit 1987;3: 25–30.
2. Tuman KJ, Spiess BD, McCarthy RJ, Ivankovich AD. Comparison of viscoelastic measures of coagulation after cardiopulmonary bypass. Anesth Analg 1989;69:69–75.

Palliative Intubation for Dysphagia

To the Editor:

I would like to commend Liakakos, Ohri, Townsend, and Fountain, on their article "Palliative intubation for dysphagia in patients with carcinoma of the esophagus" [1] for addressing a continuing difficult clinical problem, ie, management of unresectable malignant esophageal obstruction. As is commonly known, these are extremely sick, terminal patients with serious and refractory medical problems. Sometimes the situation is further exacerbated by a disabling respiratory-esophageal fistula. Thus, any attempt to palliate these unfortunate individuals is truly worthwhile [2].

Although Liakakos and associates' attempts are indeed laudatory, unfortunately their results are not. Their reported morbidity (34.2%) and mortality (6.7%) for insertion of an endoesophageal prosthesis are high. Furthermore their incidence of perforation (10.5%) and tube migration (6%) is also excessive.

As an ardent advocate of endoesophageal prosthesis [3, 4] I would like to offer two suggestions to minimize their complications. Initially I believe the traction technique is far simpler and offers the advantage of guiding the prosthesis through obstructive lesions rather than pushing it, and in many situations, seating it "blindly." Although this technique is not complication-free, our perforation rate is only 3%. Second, we routinely suture the prosthesis to the anterior gastric wall with nonabsorbable sutures. Employing this modification, we have never experienced tube migration.

Adhering to these principles in a similar group of patients, our present results are significantly better: morbidity, 15%; and mortality, 4%. Because these patients are extremely ill, any mishap in an attempt to palliate them frequently worsens their already unfortunate remaining days. Hopefully these constructive criticisms will assist in even further improving the management of a truly devastating disease process.

Lewis Wetstein, MD

143 South St
Freehold, NJ 07728

References

1. Liakakos TK, Ohri SK, Townsend ER, Fountain SW. Palliative intubation for dysphagia in patients with carcinoma of the esophagus. Ann Thorac Surg 1992;53:460–3.
2. Wetstein L, Shubert ML, Kirby DF, et al. A prospective evaluation of endoscopic Nd:YAG laser therapy in squamous cell carcinoma of the esophagus. Chest 1987;92:62S.
3. Wetstein L, Brenner A. Management of unresectable malignant esophageal obstruction. Milit Med 1990;155:324–6.
4. Wetstein L, Kirby DF, Smith WK, et al. Treatment of malignant esophagorespiratory fistula. Clin Res 1987;35:14A.

Reply

To the Editor:

We are interested to read Dr Wetstein's views on the treatment of advanced esophageal carcinoma. It is clear that we share his objectives although our methods differ slightly. Dr Wetstein's technique presumably involves the performance of a small laparotomy, and it is precisely to avoid this that we and many others have over the past 15 years turned from traction to pulsion intubation. Much has been written about the trauma of access in the context of minimally invasive operation, and the same advantages in terms of early mobilization and discharge from hospital apply to endoscopic procedures. We do not deny that the procedure carries a certain morbidity and that the problem of tube dislodgment occurs too frequently. We anticipate, however, that the development of other new techniques such as laser therapy and brachytherapy will enable us to offer a full spectrum of palliative measures in appropriately selected patients with inoperable esophageal carcinoma, without recourse to techniques that we have largely given up.

Finally we cannot accept Dr Wetstein's contention that his mortality at 4% is "significantly" better than ours at 6.7%, as the populations have not been compared.

Theodore K. Liakakos, MD
Sunil K. Ohri, FRCS
Edward R. Townsend, FRCS
S. William Fountain, FRCS

Harefield Hospital
Harefield, Middlesex UB9 6JH
England

The Blue Man Phenomenon

To the Editor:

We have recently demonstrated significant transcutaneous iodine absorption after aqueous povidone iodine skin preparation in infants undergoing cardiac operation [1]. Mediastinal irrigation in the treatment of mediastinitis has also been associated with iodine toxicity [2], and we would now like to draw attention to another mode of iodine absorption of interest to thoracic surgeons.

A 26-year-old man was admitted to our unit with a history of recurrent left-sided pneumothorax. He was allowed a shower and prepared for the operating theater. Only a small area of skin was cleaned (albeit with povidone iodine), and he duly underwent an uncomplicated thoracoscopy and talc pleurodesis.

Two hours later it was noticed that his entire body had become bright blue from the neck downward. He was not cyanosed and was otherwise well. When his skin was wiped with a swab, the blue color stained the swab, leaving a white streak on his skin. Interestingly, 1 hour later the white streak had again become blue, suggesting that some substance was being secreted by the skin. Over the next 24 to 48 hours his skin color returned to normal.

The talc used for pleurodesis in our hospital has traditionally been mixed with iodine to enhance sterility. We explain the phenomenon described above by postulating that this iodine had been absorbed through the pleura into the bloodstream and then secreted in the sweat (which is known to be a vehicle for iodine excretion). Any appropriate substance present on his skin could then react with iodine to produce a blue color. Starch is the most common material associated with this, although it cannot be implicated here as the bed linen was starch-free. However, detergents, shower gels, or washing solutions could produce the same effect, and in this case shower gel may have been responsible.

The observation of a markedly elevated plasma total iodine concentration 18 hours after thoracoscopy (2,120 nmol/L, approximately twice the upper limit of our previously measured reference range) lends support to this hypothesis, as although povidone iodine was used for skin preparation the area prepared was very small and transcutaneous absorption in an adult would be unlikely to account for this very marked and rapid response.

In view of the toxicity of high plasma iodine concentrations [1], the thoracic surgeon should be aware that topical [1], mediastinal [2], and intrapleural iodine-containing compounds should be used sparingly and with caution.

Ian M. Mitchell, FRCS
Nigel R. Saunders, FRCS
Robert D. Paton, PhD
Robert W. Logan, FRCP(Glasg)

Department of Cardiac Surgery
Leeds General Infirmary
Great George St
Leeds LS1 3EX
England

References

1. Mitchell IM, Pollock JCS, Jamieson MPG, Fitzpatrick KC, Logan RW. Transcutaneous iodine absorption in infants undergoing cardiac operation. Ann Thorac Surg 1991;52:1138–40.
2. Glick PL, Guglielmo BJ, Tranbaugh RF, Turley K. Iodine toxicity in a patient treated by continuous povidone-iodine mediastinal irrigation. Ann Thorac Surg 1985;39:478–80.

Minimal Hemodilution and Optimal Potassium Use During Normothermic Aerobic Arrest

To the Editor:

We previously reported on our experience with continuous normothermic blood cardioplegia [1]. Standard cardiopulmonary bypass techniques were used and cardiac arrest was obtained employing 4 portions of blood to 1 portion of Fremes' solution [2]. Despite the great advantages of this technique over other strategies of myocardial preservation, the employed Fremes' solution displayed several disadvantages in our experience, such as a low oxygen carrying capacity, excessive systemic hemodilution during prolonged cross-clamping of the aorta, unnecessary potassium overload in long operations, and inability to reduce the levels of ionized calcium in the cardioplegia during operations for acute ischemia [3]. To circumvent these pitfalls, we describe a new cardioplegia delivery system aiming to optimize the oxygen delivery and reduce the systemic hemodilution or potassium overload.

Blood for cardioplegia is withdrawn from the arterial line of the cardiopulmonary bypass circuit. Undiluted cardioplegic components are delivered directly into the blood cardioplegia line, using two syringe infusion pumps, one for potassium chloride and the other for citrate-phosphate-dextrose plus magnesium (Fig 1). Because the pH of the blood cardioplegia is usually greater than 7.4, tromethamine was not added. While the antegrade induction is achieved with 300 ± 50 mL/min for 1 to 2 minutes, continuous retrograde maintenance cardioplegia is generally delivered, depending on cardiac hypertrophy, at 200 ± 50 mL/min. Great care is taken to maintain coronary sinus pressure less than 50 mm Hg. To maintain constant the cardioplegia composition (potassium, magnesium, and ionized calcium levels), any variation in the blood cardioplegia pump output necessitates modification of the rate of delivery of cardioplegic components.

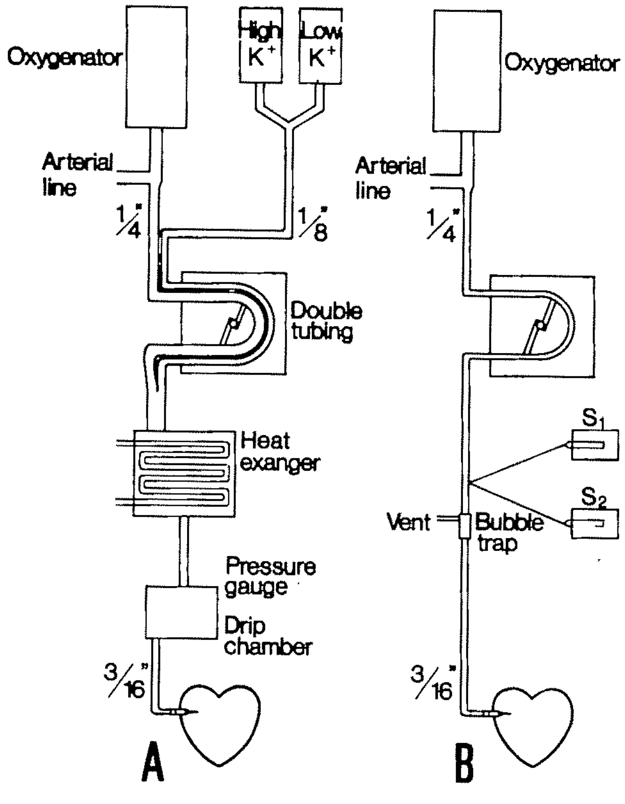


Fig 1. (A) Original normothermic blood cardioplegia delivery system. (B) Simplified normothermic blood cardioplegia delivery system. (S_1, S_2 = syringes 1 and 2.)

To achieve the desired composition of the blood cardioplegic solution (K$^+$: high [for induction] = 25 mmol/L; low [for maintenance] = 8.5 to 9 mmol/L; Mg = 3 to 3.5 mmol/L, and ionized calcium = 0.5 mmol/L), we calculated normograms for the rate of delivery of the two syringe infusions. For the K$^+$ pump (syringe 1), the infusion rate at a given cardioplegia roller pump output was obtained using the following formula:

$$q1 = 60\,[Q(p - k)]/K - p,$$

where q1 represents the estimated rate of infusion of undiluted KCl into the blood cardioplegia line in mL/h, 60 the convertor factor of mL/min to mL/h, Q the oxygenated blood output from the cardioplegia pump in mL/min, p the desired concentration of K$^+$ in the blood cardioplegia (high = 25 mmol/L; low = 8.5 to 9 mmol/L), k the patient's serum K$^+$ level expressed in mmol/L, and K the concentration of K$^+$ in undiluted KCl solution. If cardiac activity returns during maintenance cardioplegia, the infusion rate of the potassium pump is enhanced until electromechanical quiescence is again achieved. Because the maintenance of the aerobic arrest varies from patient to patient, the output of syringe 1 may be adapted to avoid unnecessary K$^+$ overloads, without affecting the myocardial oxygenation.

For the $MgSO_4$ + citrate-phosphate-dextrose pump (syringe 2), the solution includes 30 mL of citrate-phosphate-dextrose and 12 mmol of Mg at 10%. The syringe's output (q2, mL/h) is obtained according to the following formula: $q2 = 0.48 \times Q$, where 0.48 represents the factor that allows us to obtain a Mg concentration of 3.5 mmol/L in the blood cardioplegia and to deliver a citrate-phosphate-dextrose concentration equivalent to the Fremes' solution.

So far, we have performed 150 valve, coronary, or combined valve and coronary procedures using the described cardioplegic technique. Comparing the obtained data with those of our previous experience [1], there were remarkable differences in the hemoglobin level in the blood cardioplegia (9.1 ± 0.4 g/dL versus 6.8 ± 0.4; $p < 0.05$), the serum K$^+$ level at the end of the cardiopulmonary bypass (4.4 ± 1.5 versus 5.5 ± 1.8 mmol/L; $p < 0.05$), and the volume of crystalloid used (135 ± 7.1 versus 1,717 ± 85 mL, $p < 0.001$).

The output of syringe 1 depends on the blood levels of K$^+$, which varies from patient to patient and during aortic cross-clamping. The described technique avoids the use of a heat exchanger in the cardioplegic circuit because the perfusate is constantly maintained at 37°C and the small volume of crystalloid added does not lead to substantial heat loss. The elimination of heat exchanger and double tubing further reduces the priming volume (see Fig 1). Moreover, this system permits the use of the strategy suggested by Allen and associates [3] for acute evolving infarctions to obtain lower levels of ionized calcium in the cardioplegia by increasing the infusion rate of syringe infusion pump 2.

Although these observations require confirmation, the described system is simple and provides reliable cardioplegic composition, allowing manipulation of potassium and calcium levels as desired.

Daniel Le Houerou, MD
Ajoy I. Singh, MD
Mauro Romano, MD
Victor Martin, MD
Arrigo Lessana, MD

Department of Cardiovascular Surgery
Hopital Europeen de Paris "La Roseraie"
120 Avenue de la Republique
93300 Aubervilliers, Paris
France

References

1. Lessana A, Romano M, Singh AI, et al. Beyond cold cardioplegia. Ann Thorac Surg 1992;53:666–9.
2. Lichtenstein SV, Ashe KA, Delati H, et al. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
3. Allen BS, Ocamato F, Buckberg GD, et al. Studies of controlled perfusion after ischemia. Immediate functional recovery after 6 hours of regional ischemia by careful control of conditions of reperfusion and composition of reperfusate. J Thorac Cardiovasc Surg 1986;92:621–35.

Rapid Transfusion After Aortic Decannulation

To the Editor:

We read with interest the report of Davtyan and Guyton [1] describing a technique for rapid transfusion after aortic decannulation. The importance of this simple method is to avoid a massive blood loss when an accident occurs during the aortic decannulation maneuver. The described technique seems to be a more effective method than the one previously published [2], as the rapid transfusion could be accomplished without removing the aortic cannula.

Since 1974, we have used, at our institution, an original method with an additional connection interposed between the arterial and venous lines (Fig 1A). This connecting tube, closed during cardiopulmonary bypass, can be opened just by removing a clamp with different purposes (eg, aortic air removal [3] and testing the mitral valve after repair [4]).

Our simple and secure method is also routinely used for rapid transfusion through the venous cannula by clamping the aortic cannula and declamping the connecting tube (Fig 1B) without additional maneuvers in the circuit.

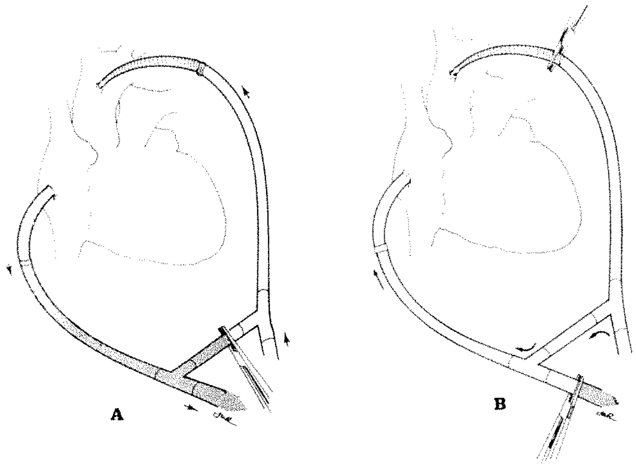


Fig 1. Modified cardiopulmonary bypass system. (A) The clamped connecting tube assures the standard circuit (arrows). *(B) The clamped arterial cannula and distal venous line establish rapid transfusion when the connecting tube is declamped* (arrows).

Jose M. Bernal, MD
Jose M. Rabasa, MD
Jose M. Revuelta, MD

Cardiovascular Surgery Department
Hospital Universitario Valdecilla
Universidad de Cantabria
39008 Santander, Spain

References

1. Davtyan HG, Guyton RA. Rapid transfusion after aortic decannulation. Ann Thorac Surg 1992;53:351.
2. Elami A, Fishman NH, Merin G. Rapid autotransfusion during complicated aortic decannulation. Ann Thorac Surg 1988; 45:696.
3. Gallo I, Martinez R, Ruiz B, Duran CMG. A simple technique for removal of residual air after cardiopulmonary bypass. Thorac Cardiovasc Surg 1982;30:117–9.
4. Pomar JL, Cucchiara G, Gallo I, Duran CMG. Intraoperative assessment of mitral valve function. Ann Thorac Surg 1978; 25:354–5.

CLASSIFIED ADVERTISEMENTS

Classified advertisements for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Art Carlucci, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010 (telephone: (212) 633-3806; facsimile: (212) 633-3820). All advertisements are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.50 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $18.00 per insertion for box number advertisements.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Advertisement orders should be for a maximum of 6 months; advertisements may be renewed for up to 6 months at a time. Advertisement copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery,* Desk Editorial, Classified Advertisements, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3853). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the advertisement. To respond to an anonymous advertisement, write to Box Number, *The Annals of Thoracic Surgery,* Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Cardiovascular and thoracic surgeon to join established 2-man private practice in Southeast. Practice includes cardiac and general thoracic surgery. Must be board certified or eligible in thoracic and cardiovascular surgery. Prefer candidate who has recently completed his/her training. Please respond with curriculum vitae.

Please respond to Box 696. 696E/J

Thoracic and cardiovascular surgeon with emphasis on pediatric/neonate cardiac surgery and cardiac transplantation is needed by a full-service thoracic and cardiovascular surgery group on the west coast. Must have ABTS certification. Excellent salary and benefits package. Please respond with curriculum vitae and case list.

Please respond to Box 702. 702E/J

Cardiovascular and thoracic surgeon to join established three-man clinic practice in Arkansas. Practice includes thoracic, cardiac, and vascular surgery. Must be board eligible and board certified in thoracic and cardiovascular surgery.

Please send CV to Donald L. Patrick, MD, 1500 Dodson Ave, Fort Smith, AR 72901; (501-782-2071). 717F/K

Cardiothoracic/vascular surgeon: board certified in general and thoracic surgery. Minimum of 2 years of practice experience. Very active private multispecialty practice. Located in western Pennsylvania. Salary leading to full partnership. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to Box 719. 719F/K

Thoracic and vascular surgeon, BE/BC, to join active (noncardiac) thoracic and vascular practice in Pittsburgh, PA. Please respond with curriculum vitae and details of experience.

Please respond to Box 720. 720F/K

Cardiothoracic surgeon, board certified/eligible, wanted to join established practice in northwest Indiana (very near Chicago). Excellent salary. Please respond with curriculum vitae.

Please respond to Box 723. 723F/K

Cardiothoracic and vascular surgeon, BE/BC, to join a well-established, very busy private practice in New England. Medical school affiliation. Excellent salary and benefits with eventual partnership.

Please respond to Box 727. 727G/L

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 728. 728G/L

Cardiothoracic surgeon, BE/BC, wanted to join established practice in mid-Michigan group of two. Ninety percent of practice is adult surgery and ten percent is general thoracic surgery. Respond with CV and names of references.

Please respond to Box 735. 735G/L

Board eligible or certified cardiovascular and thoracic surgeon needed to join a busy practice in the Southeast. Excellent salary and fringe benefits leading to partnership.

Please respond to Box 737. 737H/A

Chief, Division of Cardiothoracic Surgery: The School of Medicine and Biomedical Sciences of the State University of New York at Buffalo is seeking a highly qualified individual to lead their Cardiothoracic Division. This position will provide leadership for a citywide academic affiliated system, which includes six university teaching hospitals. The new Chief will be responsible for the overall supervision of clinical, administrative, research, and educational activities within this citywide division of cardiothoracic surgery. Qualified candidates will be strong, committed academic leaders with outstanding clinical, teaching, and research skills.

Please contact Jeanne Dowrick, Fulton, Longshore and Associates, Inc, 527 Plymouth Rd, Plymouth Meeting, PA 19462; (800) 346-8397 or (215) 834-6780. The State University of New York at Buffalo is an affirmative action/equal opportunity employer. 738H/J

Cardiovascular and thoracic surgeon, BE/BC, to expand new open heart program. Practice includes vascular and thoracic surgery. Located on the west coast of Florida. Send CV and references.

Please respond to Box 739. 739H/J

Cardiovascular surgeon, board certified/eligible, wanted to join an established cardiovascular program in Southeast performing over 600 adult open heart operations per year. Excellent salary and benefits leading to full partnership. Please send detailed CV.

Please respond to Box 742. 742H/J

Cardiothoracic vascular surgeon, board certified or board eligible, to join well-established, busy one-man private practice in Midwest. Salary leading to partnership. Please send CV and references.

Please respond to Box 743. 743H/J

BC/BE cardiovascular and thoracic surgeon wanted to join busy two-member group in Fort Lauderdale, Florida. Recent US medical graduate preferred.

Please send CV to I. Tabry, MD, 2773 NE 37th Drive, Fort Lauderdale, FL 33308 ((305) 561-9781 after 9:00 PM). 746H/A

Cardiothoracic and vascular surgeon, board eligible or certified, to join 2-man private practice in Ft. Lauderdale, Florida.

Please send CV to Salem M. Habal, MD, 4800 NE 20th Terrace #107, Ft. Lauderdale, FL 33308; (305) 771-3220. 748H/A

Cardiothoracic surgeon, BC/BE, wanted to join adult cardiac surgery program in the South. Solo practice is very busy serving as regional referral center. First-rate medical facilities, liberal compensation package, and warm hospitality await you! Please send CV.

Please respond to Box 752. 752I/L

Cardiac surgeon wanted to join established private practice in upstate New York, primarily adult cardiac. Board certified or eligible required. New or recent graduate preferred. Please send CV and reference.

Please respond to Box 753. 753I/K

Cardiothoracic and vascular surgeon, BE/BC, to join small, quality one-man practice. Salary leading to partnership or independent practice. Please send CV and references.

Please respond to Box 756. 756I/J

Thoracic/cardiovascular surgeon: three-man group in suburban New York doing general thoracic and peripheral vascular surgery desires new graduate of approved thoracic program with training in vascular surgery. Please respond with CV.

Please respond to Box 758. 758I/B

Cardiac, thoracic, and vascular surgeon needed for busy surgical group in Southeast. Outstanding income, benefits, working conditions, and quality of life. Excellent opportunity for recent trainee or experienced surgeon.

Please respond to Box 762. 762I/K

Cardiovascular and thoracic surgeon: BE/BC wanted to join an established, busy private practice in the Midwest. Peripheral vascular expertise desirable. Recent graduate of a university program preferred. Salary leading to full partnership. Please respond with curriculum vitae and references.

Please respond to Box 763. 763I/B

Cardiothoracic surgeon: Board certified/eligible and recently trained, to join an established and expanding private practice of cardiac surgery.

Please respond with curriculum vitae and details of experience to John M. Postel, MD, Chief of Cardiac Surgery, Cedars Medical Center, 1400 NW 12 Ave, Miami, FL 33136. 765I/K

Cardiothoracic surgeon—to join a 3-man private practice in cardiac, thoracic, and vascular surgery in the Great Lakes region. Must be board certified or eligible. Recent graduates considered. Send curriculum vitae.

Please respond to Box 766. 766I/K

BC/BE surgeon wanted to join adult cardiac and thoracic practice in Southeast. Approximately 300 cases per year. Relaxed environment. Include CV with response.

Please respond to Box 768. 768J/K

Pittsburgh—BE/BC cardiothoracic surgeon: Outstanding opportunity to join established 2-person cardiothoracic surgery group affiliated with large teaching hospital. High-volume practice includes comprehensive range of adult cardiovascular and thoracic procedures. Associate will play an active role at main hospital and assist group to develop suburban patient base. Attractive partnership potential.

Please reply to Daniel Stern & Associates, The Medical Center East, 211 North Whitfield St, Suite 240, Pittsburgh, PA 15206; FAX (800) 892-2781 or call (800) 438-2476. 769J

Cardiothoracic surgeon—BE/BC—to join 2-man practice in South performing adult cardiac, thoracic, and vascular surgery. Surgeon finishing training or recent graduate preferred.

Please respond to Box 770. 770J/A

Cardiothoracic surgeon, BE/BC, to join expanding practice of cardiothoracic surgery with Rhode Island Hospital Surgery Foundation, Inc, the surgical faculty practice group for the 719-bed hospital and major affiliate of Brown University School of Medicine. Excellent clinical and investigational facilities available with ample opportunities for clinical or basic science research. Solid general surgical residency with active medical student participation. Minimum of 3–5 years of experience with eligibility for clinical faculty appointment.

Send curriculum vitae to William R. Thompson, MD, Surgeon-in-Chief, Department of Surgery, Rhode Island Hospital, 593 Eddy St, Providence, RI 02903. 771J

Cardiothoracic and vascular surgeon to join a busy and well-established 3-man practice in mid-Michigan. Applicant should be board certified or eligible in thoracic and cardiovascular surgery. We prefer a candidate who has recently completed his or her training. Competitive salary leading to early partnership, with excellent benefits and working conditions. Please respond with CV.

Please respond to Box 772. 772J/L

Cardiothoracic surgeon, BE/BC, to join busy 3-man cardiothoracic private practice in Manchester, NH. Salary and benefits leading to partnership.

Interested applicants should send CV to Benjamin M. Westbrook, MD, 100 McGregor St, Manchester, NH 03102-3770. 775J/C

BE/BC cardiovascular and thoracic surgeon wanted to join expanding practice in the Southeast area. Full benefit package leading to partnership. Respond with CV and references.

Please respond to Box 777. 777J

Cardiovascular and thoracic surgeon: Multispecialty group seeks second surgeon for balanced practice of adult cardiac, thoracic, and peripheral vascular surgery. Recent graduate preferred. Located on Florida's Gulf Coast, Tampa Bay area.

Please send response to H. Charles Campbell, MD, Diagnostic Clinic, 1551 West Bay Dr, Largo, FL 34640. 778J/L

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in mid-Michigan. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Please respond to Box 779. 779J/C

Cardiothoracic surgeon: BC/BE adult cardiothoracic surgeon wanted to join busy, established practice of four physicians. Physician will join large multispecialty group in metropolitan community of 130,000 in the upper Midwest. Affiliation with medical school and surgery residency available.

Please respond to Kathleen Toft, Director, Physician Recruitment, 737 Broadway, Fargo, ND 58123; or call 1-800-437-4010. 780J/L

Assistant surgeon: Cardiac, thoracic, or general surgeon with cardiac experience to join well-established 4-man group in the Midwest. Ideal for physician who desires low stress practice. Generous salary and fringe benefits. Please send curriculum vitae.

Please respond to Box 781. 781J/L

Cardiothoracic surgeon: Wanted to join a busy, well-established practice located in the Midwest. Prefer recent graduate, must be board certified or eligible, medical school affiliation possible. Respond with curriculum vitae.

Please respond to Box 782. 782J/L

SITUATIONS WANTED

General thoracic surgeon (BC), mature, looking for community with need, preferably Northeast or Southwest and group practice. Recent 10 years general surgical experience (BC) including laparoscopy.

Please respond to Box 741. 741H/A

Cardiovascular surgeon—34 y/o, ABTS, AOA, university trained—one year of clinical practice. Wishes to relocate to medium size community.

Please respond to Box 760. 760I/L

American born and trained, ABTS certified, 43-y/o cardiac surgeon wishes to relocate. Extensive experience with elective and emergent cardiac surgery, thoracic and vascular surgery.

Please respond to Box 773. 773J/K

Adult and pediatric cardiothoracic surgeon, 39, ABS, ABTS, recently trained and experienced, wishes to relocate to private or group practice. CV and references on request.

Please respond to Box 774. 774J

FELLOWSHIPS

Surgical residents/fellows—Clinical residency/fellowship positions available in adult and pediatric cardiothoracic surgery. Large volume of cases. New Jersey license required. Excellent salary and benefits.

Please contact Lynn B. McGrath, MD, Chairman, Department of Surgery, Deborah Heart and Lung Center, 200 Trenton Rd, Browns Mills, NJ 08015; (609) 893-6611, Ext 359. 653A/J

Lung transplant fellowship: The Joint Marseille-Montreal Lung Transplant Program offers fully qualified surgeons an opportunity to spend 6 months each in Montreal, Canada, and Marseille, France. Fellows will participate in recipient and donor selection, procurement, transplantation of single lungs, double lungs, and heart/lungs as well as early and long-term care of patients. The fellowship includes an opportunity to develop in-depth knowledge of the basic science of transplantation through intense courses given at McGill Center for Clinical Immunobiology and Transplantation. Hands-on experience is provided for management of airway problems including bronchial laser and stent therapy under the supervision of Prof J. F. Dumon. An additional year of basic research experience is optional.

Please respond to Dr H. Shennib, Director, Montreal Lung Transplant Program, Montreal General Hospital, 1650 Cedar Ave, Rm L9 117, Montreal, Que, Canada H3G 1A4. 736H/J

Fellowship in cardiovascular surgery: Fellowship available in cardiovascular surgery from July 1, 1993, to June 30, 1992, located in southern California. Suitable for individuals waiting to enter or who have completed a thoracic surgery residency. California state medical licensure a necessity.

Please send CV, references, and clinical experience to Cardiovascular Surgery Fellowship, PO Box 232348, San Diego, CA 92193. 776J/K

THE SOCIETY OF THORACIC SURGEONS

Surgical Video Library

½-inch VHS format
nternational formats available

$25.00 eac
(includes shipping and handli

---

9 Titles Available:

- Esophageal Manometry — Indications, Technique and Computerized Assessment (Tom R. DeMeester)
- En Bloc Resection of A Superior Sulcus Tumor (Robert J. Ginsberg)
- Composite Valve Graft Replacement of Ascending Aorta (Cabrol Technique) and Transaortic Replacement of Mitral Valve (E. Stanley Crawford)
- Graft Replacement of Thoraco-Abdominal Aortic Aneurysm (E. Stanley Crawford)
- Aortic Valve Replacement with Aortic Allograft (Donald B. Doty)
- Multiple Internal Mammary Artery Grafts (Alfred J. Tector)
- Extended Endarterectomy for Left Anterior Descending Disease (W. Dudley Johnson)

NEW!

- Sleeve Lobectomy (Douglas J. Mathisen)
- Tracheal Resection (Douglas J. Mathisen)

Videos can be ordered by mail for $25.00 each* (includes shipping and handling).

Please send order along with payment to:

The Society of Thoracic Surgeons
P.O. Box 809285
Chicago, IL 60611

Allow 4-6 weeks for delivery

International formats (standard PAL and SECAM only) are available at $50.00 eacł including production and shipping. **Please allow 12 weeks for delivery.**

MAYO CLINIC

Mayo Clinic is seeking a thoracic and cardiovascular surgeon to join their group medical practice in Jacksonville, Florida. Candidates should be eligible for or certified by the American Board of Thoracic Surgery or the equivalent if trained abroad. Clinical expertise in general thoracic and adult cardiac surgery is required. Position has academic appointment appropriate for surgeon's qualifications. Forward curriculum vitae and name/addresses of three references to:

Peter C. Pairolero, MD, Chair
Division of Thoracic &
Cardiovascular Surgery
Mayo Clinic
200 First Street Southwest
Rochester, MN 55905

Mayo Foundation is an affirmative action and equal opportunity educator and employer.

CARDIOTHORACIC SURGERY

The Division of Cardiothoracic Surgery at Tulane University School of Medicine is seeking applicants for a full-time academic position at the assistant/associate professor level. Applicants should be BC/BE in cardiothoracic surgery. The Division sponsors a fully approved graduate education program in cardiothoracic surgery with involvement at Tulane University Hospital, Charity Hospital and VA Medical Center.

The individual sought for this position should have an interest in academic surgery and have demonstrated expertise in research. Recommendations and correspondence should be directed to:

John D. Pigott, M.D.
Director of Cardiothoracic Surgery
Tulane University School of Medicine
1430 Tulane Avenue
New Orleans, LA 70112

EOE/AA

THORACOSCOPY FOR THORACIC SURGEONS

Pericardiectomy, Blebectomy, Sympathectomy, Pulmonary Resection

These two-day advanced courses consist of four hours of didactics and 11 hours of hands-on laboratory. The techniques of thoracoscopic vagotomy, wedge resection, node dissection and other advanced procedures will be taught in detail. In addition, special emphasis will be placed on developing skills in thoracoscopic suturing and stapling techniques.

COURSE DIRECTOR	COURSE MODERATOR
Karl A. Zucker, M.D.	Mark J. Krasna, M.D.

FACULTY INCLUDES
Thomas Daniels, M.D.
Richard Heitmiller, M.D.
Rodney Landreneau, M.D.
Joseph Locicero, M.D.

The faculty is skilled in the use of hand instrumentation for the advanced thoracoscopic procedures. The operating stations are directed by thoracic surgeons who bring a wealth of clinical experience to the "hands-on" classroom.

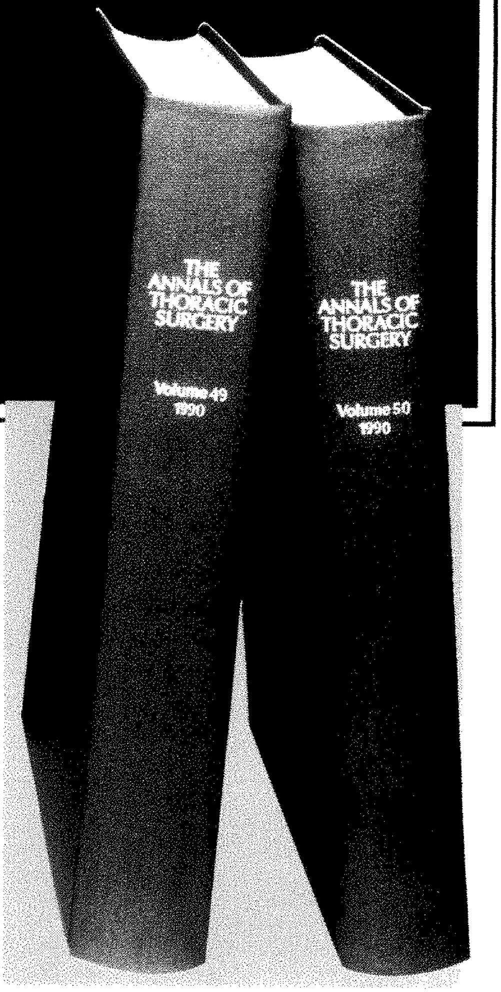
Medcom Management International, Inc.
(410) 321-5481

LOCATION
United States Endoscopy Laser Institute
Baltimore, Maryland

Courses are limited to 18 participants.

An invitation for current subscribers

Bound Volumes of THE ANNALS OF THORACIC SURGERY


THE ANNALS OF THORACIC SURGERY
Volume 49
1990
THE ANNALS OF THORACIC SURGERY
Volume 50
1990

Reserve your 1991 bound volumes now! As a special service to current subscribers only, **THE ANNALS OF THORACIC SURGERY** is available in bound volumes, priced at $83.00 (US) and $100.00 (International). The two volumes for 1991 (Volumes 51 and 52) are bound in blue buckram—the same high quality binding you would find in a library—with stamped lettering on the spine. These handsomely bound volumes include:

- complete author and subject indexes
- editorial content only, with all advertising removed
- sturdy bindings for durable reference

From now on, when you receive your regular monthly copy of **THE ANNALS OF THORACIC SURGERY,** don't hesitate to tear out or mark up articles of particular interest. These specially bound volumes include every issue in perfect condition to help you keep your personal library complete, organized and current.

Reserve your 1991 bound volumes by returning the order form below.

Clip and mail to: **Elsevier Science Publishing Co., Inc.** PO Box 882, Madison Square Station, New York, NY 10159

ORDER FORM

☐ Please send me bound volumes 51 & 52 for **THE ANNALS OF THORACIC SURGERY.*** Both volumes will be shipped together for a total cost of $83.00.

☐ Please send me bound volumes 49 & 50 for **THE ANNALS OF THORACIC SURGERY** from 1990. Both volumes for $83.00.

Outside the US, please add $17.00 for postage and handling.

☐ Please start my annual standing order to receive bound volumes of **THE ANNALS OF THORACIC SURGERY.** Two bound volumes automatically will be shipped together at the end of each year.

Note: *Offer available only for subscribers to **THE ANNALS OF THORACIC SURGERY.** Please allow 3-5 weeks for receipt of your bound volumes.

Please return to:
Elsevier Science Publishing Co., Inc.
P.O. Box 882
Madison Square Station
New York, NY 10159

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC

PAYMENT

Enclosed please find my: ☐ personal check ☐ bank draft

Please charge to:

☐ Visa ☐ AMEX ☐ MasterCard (issuing bank #______)

Card #____________________ Expires__________

Signature______________________________

☐ **Please bill me.** (Postage and handling will be added to orders.)

Name______________________________

Address____________________________

City_______________________________

State____________________ Zip__________

Country____________________________

Or order your bound volumes by phone

Tel. No.: *(212) 633-3950*

Fax No.: *(212) 633-3990*

X7AX

CARDIOVASCULAR-THORACIC SURGEON

BC/BE **Cardiovascular-Thoracic Surgeon** needed to join Carle Clinic Association, a 225 physician multi-speciality group practice in central Illinois. This position covers the entire range of adult cardiac, thoracic, and vascular surgery including laser surgery but excluding transplantation. Academic affiliation and research opportunities are available. Liberal fringe benefits and salary leading to equal ownership; malpractice coverage provided. Write including CV to:

Robert C. Parker, Jr., M.D.
Medical Director
Carle Clinic Association
602 West University, Urbana, Illinois 61801
call collect (217) 383-3399, FAX (217) 383-3163

UAB

Division of Cardiothoracic Surgery

Thoracic Surgeon

University of Alabama at Birmingham

The Division of Cardiothoracic Surgery at the University of Alabama at Birmingham (UAB) seeks candidates for the Head of the Section of Non-Cardiac Thoracic Surgery.

UAB Division of Cardiothoracic Surgery has a very active clinical general thoracic surgical program and a growing lung transplant program. The successful candidate must be Board Certified in Thoracic Surgery with excellent clinical skills and strong academic interests. Position is tenure-accruing with appointment at an appropriate academic level. UAB offers an excellent compensation and benefits package.

Please respond with curriculum vitae and references to:

A. D. Pacifico, M.D.
Professor and Director
Division of Cardiothoracic Surgery
University of Alabama at Birmingham
Birmingham, AL 35294-0016

UAB IS AN EQUAL OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER
WOMEN AND MINORITIES ARE ENCOURAGED TO APPLY

AVAILABLE NOW ON VIDEOTAPE

TECHNIQUES IN CONGENITAL CARDIAC SURGERY

at Children's Hospital
Boston, Massachusetts

Aldo R. Castaneda, M.D.
Frank L. Hanley, M.D.
Richard A. Jonas, M.D.
John E. Mayer, M.D.

Video Library - Volume 2

- FENESTRATED FONTAN PROCEDURE
- SINGLE PERICARDIAL PATCH REPAIR OF COMPLETE AV CANAL
- ALLOGRAFT REPAIR OF TETRALOGY OF FALLOT WITH PULMONARY ATRESIA

This videocassette provides a comprehensive intraoperative demonstration of techniques currently employed at The Children's Hospital, Boston, in the repair of complex single ventricle, complete AV canal and tetralogy with pulmonary atresia. Professional video photography, illustration and editing has insured outstanding clarity and detail. Available in VHS, Beta and 3/4" in all international formats.

PRICE: $250

Please send me **Techniques in Congenital Cardiac Surgery - Volume 2** for $250 (U.S.) plus $5 for shipping and insurance within the U.S. and $10 for shipping and insurance outside the U.S.

SIZE: ☐ VHS ☐ Beta ☐ 3/4" U-Matic

FORMAT: ☐ NTSC (USA, Canada, Japan, S. America)
☐ PAL (Europe, Asia, Australia, S. America)
☐ SECAM (CIS, Mid East, E. Europe, France)

☐ Make **CHECK** or **MONEY ORDER** payable to:
Surgical Techniques Video

☐ **CHARGE TO:** ☐ MasterCard ☐ Visa ☐ American Express
Card Number ______________________
Expiration Date ________ Signature ______________

☐ Send information on Volume I in this series.

Quantity ______ @ $250 each = $ ________
Shipping within U.S. @ $5 each = $ ________
outside U.S. @ $10 each = $ ________
TOTAL ENCLOSED (U.S. dollars) $ ________

Name ______________________
Organization ______________________
Street Address ______________________
City ______________ State/Province ______________
Zip/Postal Code ______________ Country ______________
Telephone ______________ Fax ______________

Return to:
WEISMAN VIDEO PRODUCTIONS
50 Hunt Street
Watertown, Massachusetts 02172-4625
U.S.A.

TEL: 617.926.2089 FAX: 617.926.7965

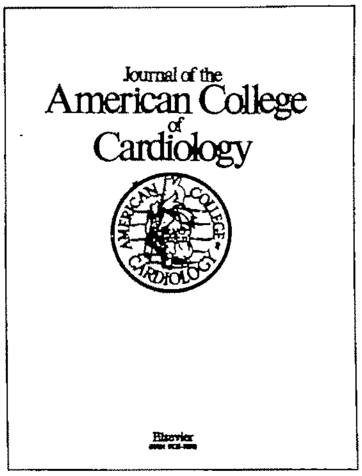
Outside USA please pay by money order in US dollar equivalent or use credit card.
Prices subject to change.
For more personalized service, please contact
Weisman Video Productions at address above.

Ten years of excellence

Journal of the American College of Cardiology

The **Journal of the American College of Cardiology, JACC,** is the leading journal in cardiology. **JACC's** timely coverage of clinically relevant information on the diagnosis and treatment of cardiovascular diseases has made it a favorite among cardiologists worldwide.

Why not join the thousands of your colleagues who have made reading **JACC** a part of their regular routine?



Read the **Journal of the American College of Cardiology** each month and you will find a superb collection of original articles, clinical reviews, special reports, and editorials at the forefront of cardiovascular medicine. **JACC's** comprehensive focus and distinguished editorial board assure you the most significant new information — information that you can apply directly to your practice.

Discover why **JACC** is the #1 journal in cardiology. Enter your subscription today and follow the most current and authoritative source on important developments in cardiology.

Journal of the American College of Cardiology
1992, Volumes 19, 20 (14 issues; 1 supplement)
ISSN **0735-1097**

Personal Rate: $94.00
Institutional Rate: $140.00
Intern/Resident/Nurse/Allied Health Rate: $58.00

For sample copies send to:
in North America
Elsevier Science Publishing Co., Inc.,
P.O. Box 882, Madison Square Station
New York, New York 10159
outside North America
Elsevier Science Publishers
P.O. Box 211, 1000 AE
Amsterdam, The Netherlands

Send subscription orders to your usual supplier or the New York address. For even faster service, call
Tel. No.: (212) 633-3950
Fax No.: (212) 633-3880

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC.

10 YEARS OF SCIENTIFIC EXCELLENCE
10
JACC

8/91 X1ET

The Annals of Thoracic Surgery

Elsevier Science Publishing Co., In
Attn: Journal Customer Service Department
P.O. Box 882, Madison Square Station
New York, New York 10159
Telephone # (212) 633-3950

Affix mailing label here.

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC.

☐ **Moving?** Please give us 6 week advance notice. Attach your old label here for better service. Pri your new address and zip code below.

☐ **Entering a New Subscription?** Please fill out the order form below.

☐ **A Problem or Query?** We can serve you best if you include yo mailing label with any correspo dence.

Name ________________
Address ________________
____
City/State ________________
Country/Zip Postal Code ________________
Specialty ________________

I am a member of:
☐ The Society of Thoracic Surgeons
☐ The Southern Thoracic Surgical Association
☐ both

New Subscriptions
☐ Please enter my 1992 subscription to **The Annals of Thorac Surgery,** ISSN 0003-4975, Volumes 53, 54 (12 issues)
☐ Institutional rate: $165.00
☐ Personal rate: $95.00*

Postage and Handling: For air delivery in the U.S., Canada and Mexico, add $80.(Subscribers outside the U.S. must add one of the following postal options: $35.00 surface delivery; $70.00 for surface air lift delivery to Europe; $85.00 for surface air delivery to Japan; or $160.00 for air delivery to the rest of the world.

Enclosed is my: ☐ personal check ☐ bank draft
Charge to: ☐ American Express ☐ VISA
☐ MasterCard (issuing bank # ________

Account # ________________ Expires ________
Signature ________________

☐ Please bill me (Orders from non-U.S. customers must be prepaid.)

Note: Personal subscriptions begin with the first month after processing of your order unless otherwise indicated. Journal rates valid through December 31, 1992.

*The personal rate is available to individuals only at home address or medical institutions.

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC.

9/91 X1GA

INTERNATIONAL SYMPOSIUM
LONDON 18-19 MARCH 1993

NEUROHUMORAL EFFECTS

OF PROFOUND HYPOTHERMIA

IN INFANT HEART SURGERY

The Royal Brompton National Heart and Lung Hospital, The University of Gothenburg and Gambro Cobe are sponsoring a two day symposium relating to the neural, systemic and other non-cardiac effects of profound hypothermia in infant cardiac surgery.

Further information can be obtained from The Postgraduate Centre, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, England.
Telephone: 071-351 8172 (24hr answering service)
Facsimile: 071-376 3442

Academic General Thoracic Surgeon

The Division of Cardiothoracic Surgery in the Department of Surgery and the H. Lee Moffitt Cancer Center & Research Institute at the University of South Florida are seeking two academic general thoracic surgeons with specific interest in thoracic oncology. One of the individuals will serve in a leadership capacity at the level of section chief.

Applicants should be board certified in Cardiothoracic Surgery with a primary interest in lung, pleural or esophageal malignancies, and be qualified to serve at the rank of assistant, associate or full professor. Experience in multidisciplinary clinical settings is desired and applicants should demonstrate a focused approach to specific areas of clinical care and research. These positions may be tenure earning.

Send Curriculum Vitae to Peter McKeown, M.D., Head, Division of Cardiothoracic Surgery, University of South Florida, or John C. Ruckdeschel, M.D., Center Director/CEO at H. Lee Moffitt Cancer Center & Research Institute. Address: Search Committee, Office of Faculty Recruitment, 12902 Magnolia Drive, Tampa, Florida 33682-0179. Deadline for receipt is October 24, 1992.

H. Lee Moffitt Cancer Center & Research Institute, adjacent to the Health Sciences Center on the University of South Florida's Tampa Campus, includes a modern 162-bed cancer facility for children and adults, a large Ambulatory Services operation, a 20-bed bone marrow transplantation program and a new research building.

H. LEE MOFFITT CANCER CENTER
& RESEARCH INSTITUTE
University of South Florida College of Medicine

Moffitt Cancer Center is an Equal Opportunity Employer
The University of South Florida is an Affirmative Action Equal Opportunity Employer

---

▲Director ICU

Mount Sinai Hospital, a University of Toronto teaching hospital, is seeking a Director of a medical-surgical ICU. The successful candidate will be responsible for directing patient care and teaching activities, and for developing research programs. Excellent opportunities exist to pursue research interests in either the clinical or laboratory setting. Send curriculum vitae and personal reply to:

E.A. Phillipson, M.D., Chairman
ICU Search Committee

Mount Sinai Hospital is an Equal Opportunity Employer

MOUNT
SINAI
HOSPITAL
600 UNIVERSITY AVENUE, SUITE 427
TORONTO, ONTARIO, CANADA M5G 1X5
(416) 586-8525 FAX: (416) 586-8350

Cardiothoracic Surgery

Seeking well-trained cardiothoracic surgeon to join a well established cardiac surgery division. Will play an important role in the education and training of medical students and surgical residents. Experience in transplantation desired.

Will provide attractive recruitment package. Medical school faculty appointment commensurate with qualifications. Strong clinical background and board certification or eligibility in cardiothoracic surgery are essential. Excellent opportunity for research.

Send C.V. to:
Jeffrey T. Sugimoto, M.D.
Chief Cardiac Surgery Division
Creighton University School of Medicine
Department of Surgery
601 North 30th Street
Suite 3740
Omaha, NE 68131
Fax: (402) 280-4593

Creighton University is an Affirmative Action/Equal Opportunity Employer

Cardiothoracic and vascular surgeon, board certified, board eligible to join a three-man practice in the Midwest.

Salary leading to full partnership.

Please send curriculum vitae.

Please respond to:
Box 784
The Annals of Thoracic Surgery
Elsevier Science Publishing Company
655 Avenue of the Americas
New York, NY 10010

Cardiovascular and thoracic surgeon: BE/BC wanted to join progressive, established cardiovascular/thoracic surgeon in a 90-doctor multispecialty group in a Big-10 University community of 100,000 with superb cultural advantages. Initial guarantee and fringes with early associateship. Subsequent income based on productivity.

For confidential consideration, please submit curriculum vitae to 663, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

INDEX TO ADVERTISERS

Baxter	A-6
Bryn Mawr Hospital	A-44
Cardiothoracic Research & Education Foundation	A-23
Carle Clinic Association	A-39
Creighton University School of Medicine	A-41
DLP	A-13
Erie County Medical Center	A-43
H. Lee Moffit Cancer Center	A-41
Intermountain Health Care	A-43
Lankenau Hospital	A-43
Mayo Clinic	A-37, A-44
MedChem	A-32
Medcom Management International	A-37
Medtronic	A-2, A-3, A-14, A-15
Mount Sinai Hospital	A-41
National Heart and Lung Institute	A-41
Promedica International	A-19, A-23
PSICOR	A-4
Scott & White Clinic	A-44
SmithKline Beecham Pharmaceuticals	A-43
Sorin	Cover 2, A-1, Cover 4
St. Jude	A-10, A-11
3M	A-17, A-18
Tulane University School of Medicine	A-37
University of Alabama at Birmingham	A-39
Vitaid	A-8
Weisman Video Productions	A-39
W. L. Gore	A-21
Classified Advertisements	A-33 through A-35

Address advertising inquiries to Art Carlucci, Elsevier Science Publishing, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3820).

VOLUME 54 NUMBER 5 NOVEMBER 1992 ISSN 0003-4975

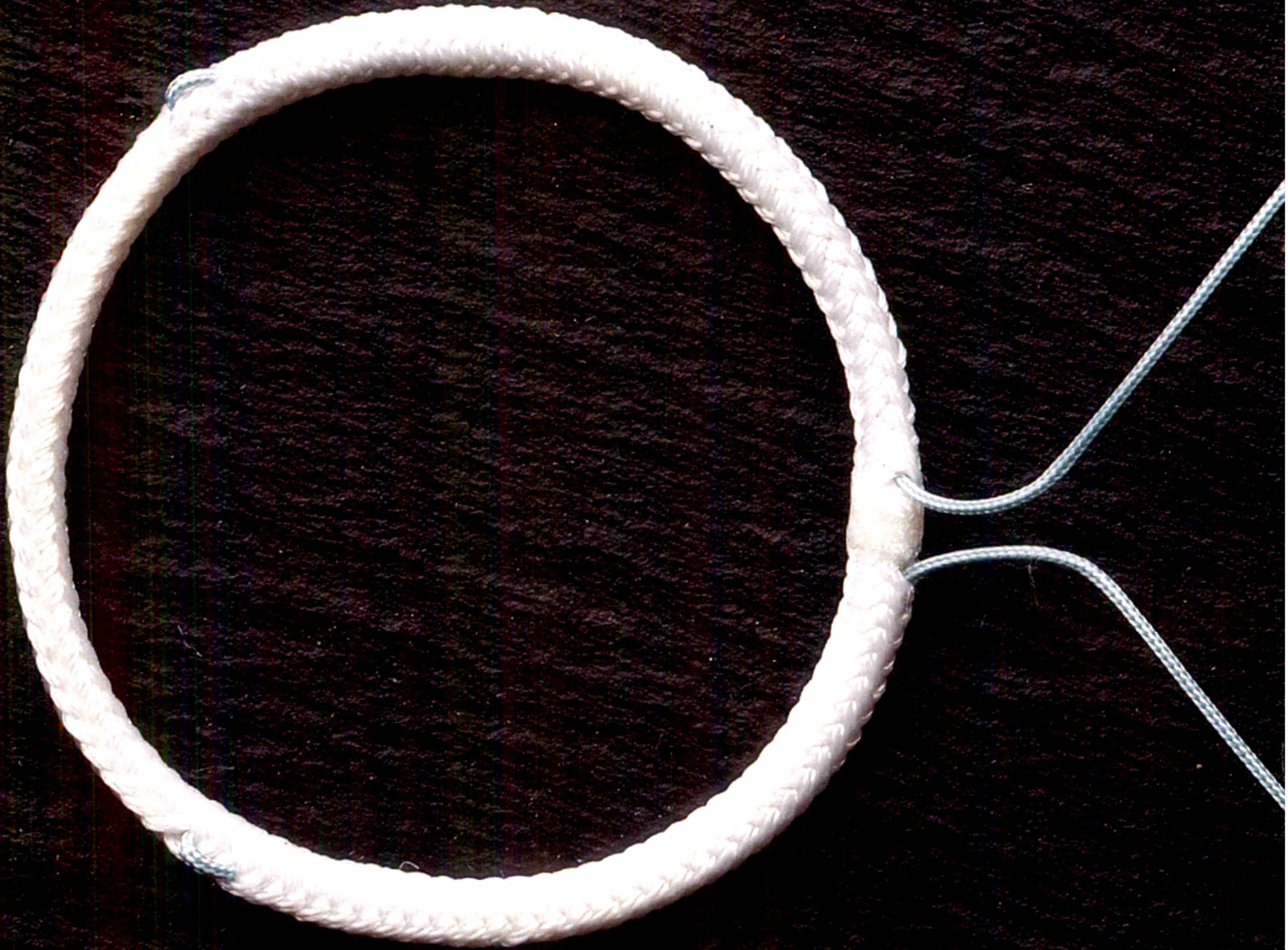
c CM

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association

TWENTY-NINTH ANNUAL MEETING OF THE SOCIETY OF THORACIC SURGEONS
JANUARY 25–27, 1993, SAN ANTONIO CONVENTION CENTER, SAN ANTONIO, TEXAS

Elsevier



SORIN BIOMEDICAL, INC. 17600 Gillette Avenue—P.O. Box 19503 Irvine, CA 92713-9503 U.S.A. Tel: (714) 250-0500, or (800) 854-3683 Fax: (714) 250-1524
DIDECO S.r.l. 41037 MIRANDOLA (MO) Italy Via Statale 12 Nord, 86—P.O. Box 87 Tel: 39/535/29811—Telex: 522388 Fax: 39/535/25229
© 1992 Sorin Biomedical, Inc. THIS DEVICE RESTRICTED TO SALE BY OR ON THE ORDER OF A PHYSICIAN.
Refer to the instructions for use provided with each device for detailed information regarding warnings, precautions and possible adverse device effects.

Volume 54 Number 5

THE ANNALS OF THORACIC SURGERY

November 1992

Contents

Editorial

Allogenic Vein as a Conduit for Coronary Artery Bypass 817

Hendrick B. Barner, MD

Thoracic Surgery Directors Association Award

Intrathecal Perfusion of an Oxygenated Perfluorocarbon Prevents Paraplegia After Aortic Occlusion 818

Robert E. Maughan, MD, Chittur Mohan, MD, Ira M. Nathan, PhD, Enrico Ascer, MD, Peter Damiani, BS, Israel J. Jacobowitz, MD, Joseph N. Cunningham, Jr, MD, and Corrado P. Marini, MD

Original Articles

Cryopreserved Allograft Veins as Alternative Coronary Artery Bypass Conduits: Early Phase Results 826

Glenn W. Laub, MD, S. Muralidharan, MD, Robert Clancy, RN, W. Jay Eldredge, MD, Chao Chen, PhD, Mark S. Adkins, MD, Javier Fernandez, MD, William A. Anderson, MD, and Lynn B. McGrath, MD

Late Results of Operation for Ventricular Tachycardia 832

Lynda L. Mickleborough, MD, Shun-ichi Mizuno, MD, Eugene Downar, MD, and Gordon C. Gray, BSc

Cardiac Retransplantation: A Viable Option? 840

Shreekanth V. Karwande, MD, R. Douglas Ensley, MD, Dale G. Renlund, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, Donald B. Doty, MD, M. Elizabeth Hammond, MD, John D. Marks, PE, and The Registry of the International Society for Heart and Lung Transplantation

continued on page A-6

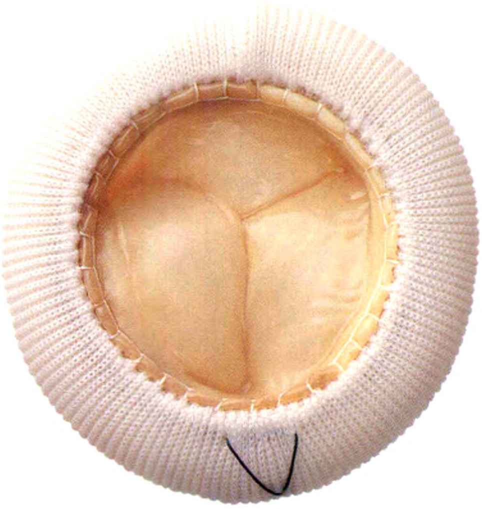
The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery*, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.

EXPERIENCE

THAT

ADDS

UP



Medtronic Hancock® Valve
Celebrating Over 20 Years

Medtronic Hall™ Valve
Celebrating 15 Years

If you would like further information, please call our toll-free physician advisory number, 1-800-328-2518. For detailed information describing intended use, warnings, precautions, and contraindications, refer to the Instructions For Use provided with the product or contact your local Medtronic representative. CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician.

[1] Data on file, Medtronic, Inc.

For over 20 years, our Medtronic Hancock® tissue valve has established a history of solid clinical experience. A history longer than any other commercially available porcine bioprosthesis.

For 15 years the Medtronic Hall™ mechanical valve has had unsurpassed durability. Its hemodynamic performance rivals that of any mechanical valve – with superior performance in the small aortic annulus.[1]

= 35

Add our experience to yours.

Years of Combined Experience

UC9202206EN
© Medtronic, Inc. 1992
All Rights Reserved

Medtronic

Continued from page A-3

Acute Rejection of Lung Allografts With Various Immunosuppressive Protocols 846

Bartley P. Griffith, MD, Robert L. Hardesty, MD, John M. Armitage, MD,
Robert L. Kormos, MD, Gary C. Marrone, MD, Steve Duncan, MD, Irvin Paradis, MD,
James H. Dauber, MD, Samuel A. Yousem, MD, and Penny Williams, MD

Improved Myocardial Ischemic Tolerance by Contractile Inhibition With 2,3-Butanedione Monoxime 852

James C. Stringham, MD, Karen L. Paulsen, BS, James H. Southard, PhD,
Barry L. Fields, MD, and Folkert O. Belzer, MD

Extracorporeal Membrane Oxygenation for Cardiac Failure After Congenital Heart Operation 861

Stanley Ziomek, MD, James E. Harrell, Jr, MD, James W. Fasules, MD,
Sherry C. Faulkner, CCP, Carl W. Chipman, RN, Michele Moss, MD,
Elizabeth Frazier, MD, and Stephen H. Van Devanter, MD

Coarctation of the Aorta in Infants: Does the Aortic Arch Grow After Repair? 869

John L. Myers, MD, Brian A. McConnell, BS, and John A. Waldhausen, MD

Postinfarct Ventricular Septal Defect Repair: Effect of Coronary Artery Bypass Grafting 876

Derek D. Muehrcke, MD, Willard M. Daggett, Jr, MD, Mortimer J. Buckley, MD,
Cary W. Akins, MD, Alan D. Hilgenberg, MD, and W. Gerald Austen, MD

Risk Analysis of Operative Intervention for Failed Coronary Angioplasty 884

A. Michael Borkon, MD, Trent L. Failing, MD, Jeffrey M. Piehler, MD,
Duncan A. Killen, MD, Marcia L. Hoskins, BS, and William A. Reed, MD

Partial Median Sternotomy for Repair of Heart Defects: A Cosmetic Approach 892

William R. Wilson, Jr, MD, Michel N. Ilbawi, MD, Serafin Y. DeLeon, MD,
William Piccione, Jr, MD, Kate Tubeszewski, RN, MSN, and Anthony F. Cutilletta, MD

Surgical Considerations in Bypassing Coronary Arteries With 100% Proximal Occlusion 894

Thomas R. McLean, MD, Lars G. Svensson, MD, PhD, Bernardo Stein, MD,
Arthur C. Beall, Jr, MD, and John I. Thornby, PhD

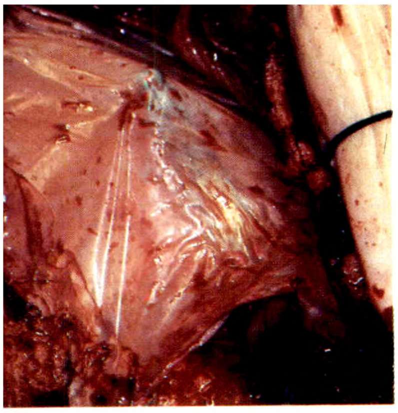
Role of Open Lung Biopsy in Diagnosing Pulmonary Complications of AIDS 898

Gregory D. Trachiotis, MD, Gordon H. Hafner, MD, William R. Hix, MD, and
Benjamin L. Aaron, MD

Tetralogy of Fallot: Favorable Outcome of Nonneonatal Transatrial, Transpulmonary Repair 903

Tom R. Karl, MD, Shunji Sano, MD, PhD, Samphant Pornviliwan, MD, and
Roger B. B. Mee, FRACS

continued on page A-8



The GORE-TEX® Surgical Membrane was removed after ten months implant duration. No epicardial reaction was noted and an effective plane of dissection was provided. Photo courtesy of S. Subramanian, M.D.

Proven Reoperative Reliability*

The GORE-TEX Surgical Membrane was removed after two months implant duration. The coronary vasculature is visible and there is a lack of adherent tissue. Photo courtesy of H. Lindberg, M.D.

An Open And Closed Case

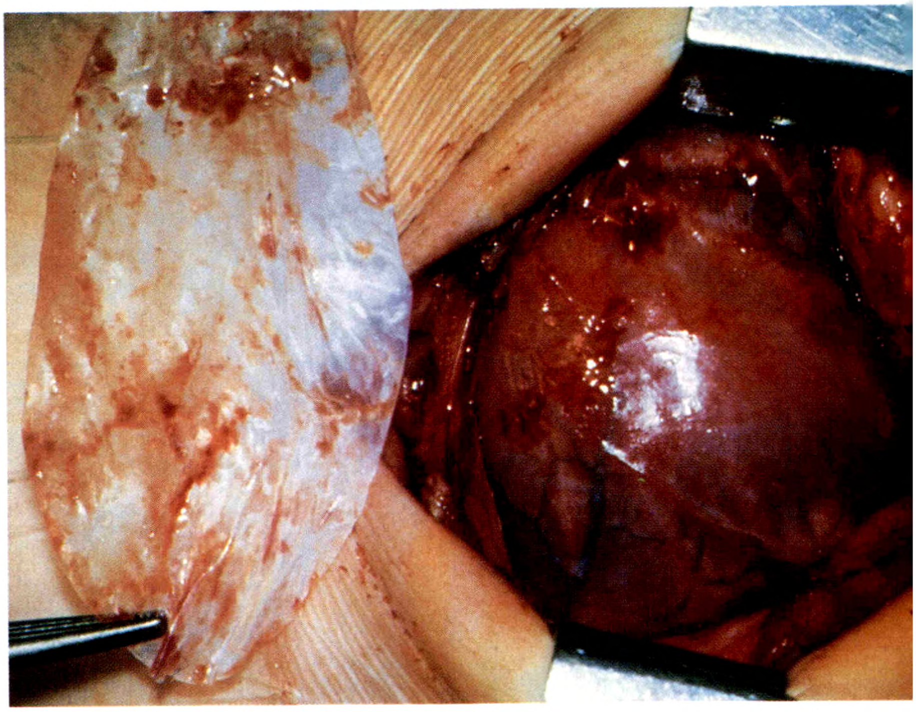
Epicardial/mediastinal adhesions are a critical reoperative challenge, at times leading to serious inherent problems such as:

- Cardiac Damage
- Catastrophic Hemorrhage
- Increased Dissection Time

Since 1976, the GORE-TEX® Surgical Membrane material has been the only pericardial substitute to consistently facilitate cardiac reoperation by providing a reliable plane of dissection and reducing adhesion formation. This minimizes the risk of:

- Cardiac Damage
- Catastrophic Hemorrhage
- Increased Dissection Time

For further information, including current available literature and recommended implant techniques, call 800-437-8181, Dept. 6-N. To order call 800-528-8763, Dept. 6-N.



☐ *Please send further information on the GORE-TEX® Surgical Membrane.*
☐ *Please arrange for a free clinical sample.*
☐ *Please have your sales representative call for an appointment.*

Name ____________________
Address ____________________
City ____________________ State __________ Zip __________
Surgical Speciality ____________________
Hospital Affiliation ____________________
Telephone ____________________

GORE-TEX® SURGICAL MEMBRANE

**Recent medical literature is available...Please call 800-437-8181 for specific information, including recommended implant technique.*

W. L. GORE & ASSOCIATES, INC.
Woody Mountain Road, P.O. Box 900, Flagstaff, AZ 86002

GORE
Creative Technologies Worldwide

®GORE-TEX is a registered trademark of W.L. Gore & Associates, Inc. © 1990 W.L. Gore & Associates, Inc.

AOTS-11-92 GSM-3R

Continued from page A-6

Benefits of Combined Balloon Pumping and Percutaneous Cardiopulmonary Bypass 908

Steven J. Phillips, MD, Robert H. Zeff, MD, Chamnahn Kongtahworn, MD, André Grignon, MD, Lawrence Barker, RN, L. A. Iannone, MD, Mark Tannenbaum, MD, Margaret H. Verhey, MD, William J. Wickemeyer, MD, Magdi G. Ghali, MD, and David F. Gordon, MD

Coronary Artery Bypass Using Internal Mammary Artery Branches 911

Jean E. Morin, MD, Giles Hedderich, MD, Normand L. Poirier, MD, John Sampalis, PhD, and James F. Symes, MD

Isolated Biventricular Working Rat Heart Preparation 915

Todd L. Demmy, MD, George J. Magovern, MD, and Race L. Kao, PhD

Effect of Prostaglandin I_2 and Superoxide Dismutase on Reperfusion Injury of Warm Ischemic Lung 921

Chojiro Yamashita, MD, Hidefumi Oobo, MD, Fukumasa Tsuji, MD, Satosi Tobe, MD, Hidehiro Yamamoto, MD, Hiroomi Nakamura, MD, Masayosi Okada, MD, and Kazuo Nakamura, MD

Comparison of 180-Degree and 360-Degree Skeletal Muscle Nerve Cuff Electrodes 925

George V. Letsou, MD, James F. Hogan, BSEE, Philip Lee, MS, Jung H. Kim, MD, Stephan Ariyan, MD, Michael L. Dewar, MD, John C. Baldwin, MD, and John A. Elefteriades, MD

Technique of Open Distal Anastomosis for Repair of Descending Thoracic Aortic Aneurysms 932

Denton A. Cooley, MD, and Robert T. Baldwin, MD

Expanding Wire Stents in Benign Tracheobronchial Disease: Indications and Complications 937

Samer A. M. Nashef, FRCS, Claire Dromer, MD, Jean-François Velly, MD, Louis Labrousse, MD, and Louis Couraud, MD

Extrapleural Pneumonectomy in the Treatment of Malignant Pleural Mesothelioma 941

David J. Sugarbaker, MD, Steven J. Mentzer, MD, and Gary Strauss, MD

Considerations in the Skeletonization Technique of Internal Thoracic Artery Dissection 947

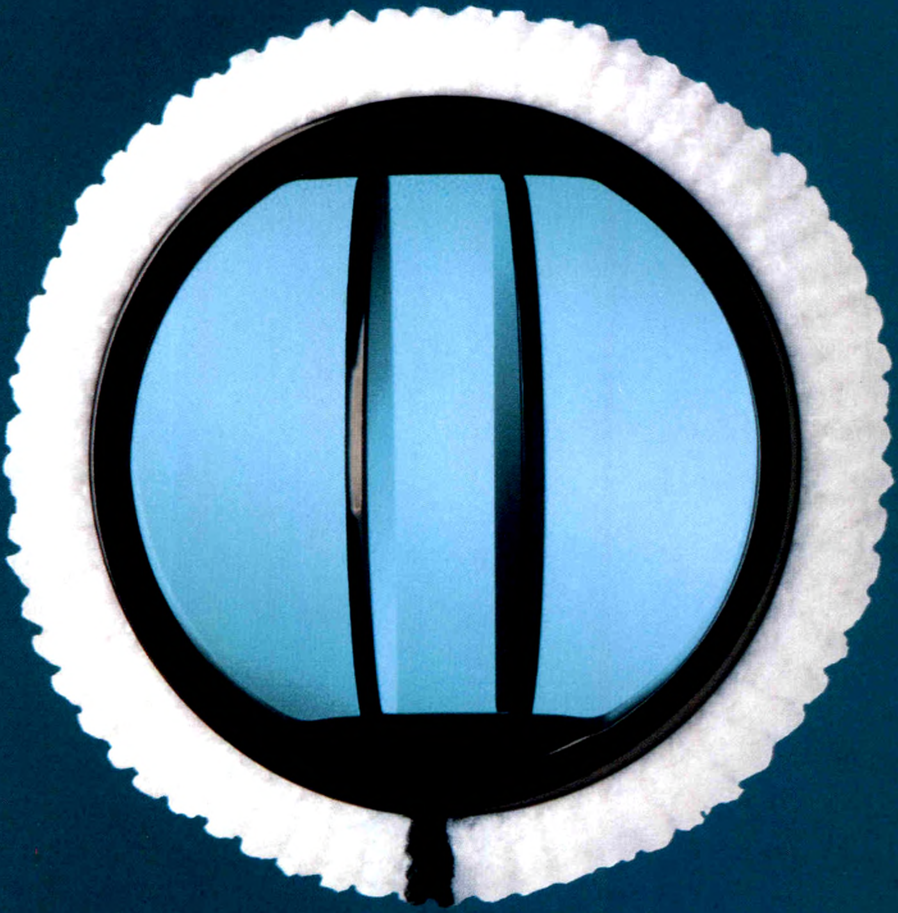
James M. Cunningham, MD, Mohammad A. Gharavi, MD, Rostam Fardin, MD, and Raymond A. Meek, MD

The Meadox-Gabbay Pericardial Xenograft: Failure of the Unicusp Principle 952

Uberto Bortolotti, MD, Paolo Ius, MD, Gaetano Thiene, MD, Marco Minarini, BS, Aldo Milano, MD, Carlo Valfrè, MD, Enrico Talenti, MD, Marialuisa Valente, MD, and Alessandro Mazzucco, MD

continued on page A-10

25%
more flow area



THE ST. JUDE MEDICAL® HEART VALVE
HEMODYNAMIC PLUS SERIES

Not Available in the USA

UNEQUALED PERFORMANCE
15
YEARS
SINCE 1977

ST. JUDE MEDICAL

Continued from page A-8

Comparison of Cardiac Output Measured by Intrapulmonary Artery Doppler, Thermodilution, and Electromagnetometry 959

Paul M. Heerdt, MD, PhD, Charles G. Pond, MD, George A. Blessios, MD, and Michael Rosenbloom, MD

Pulmonary Artery Sling 967

Ashwinikumar Pawade, FRCS, Marc R. de Leval, FRCS, Martin J. Elliott, FRCS, and Jaroslav Stark, FRCS

Case Reports

Pulmonary Artery Sling With Tracheal Stenosis: Primary One-Stage Repair in Infancy 971

Gerhard Ziemer, MD, Markus Heinemann, MD, Renate Kaulitz, MD, Joachim Freihorst, MD, Jürgen Seidenberg, MD, and Martin Wilken, MD

Surgically Created Wolff-Parkinson-White Syndrome After Fontan Operation 974

Anees J. Razzouk, MD, Robert Gow, MB, BS, John Finley, MD, David Murphy, MD, and William G. Williams, MD

True Aneurysm of the Saphenous Vein Graft Stump Associated With CABG in a Cardiac Transplant Patient 978

Robert T. Baldwin, MD, Tomas Klima, MD, O. H. Frazier, MD, James Lonquist, MD, and Branislav Radovancevic, MD

Chronic, Traumatic Pseudoaneurysm of the Ascending Aorta 980

Felipe C. Albuquerque, BA, Mark J. Krasna, MD, and Joseph S. McLaughlin, MD

Aneurysm of the Ascending Aorta After Cardiac Transplantation 983

Jean-Olivier Defraigne, MD, Olivier Vahdat, MD, Jean-Paul Lavigne, MD, Jean-Claude Demoulin, MD, PhD, and Raymond Limet, MD, PhD

Simplified Correction of Outflow Obstruction After Mitral Valve Replacement 985

Mark K. Reed, MD, and Leigh I. G. Iverson, MD

Bronchoenteric Fistula From an Infected Internal Cardioverter Defibrillator 987

Peter L. Birnbaum, MD, Samuel V. Lichtenstein, MD, PhD, William H. Noble, MD, Benjamin G. Guslits, MD, Brian D. Kenney, MD, D. Ian Soutter, MD, Anthony L. Panos, MD, Paul Dorian, MD, and David Newman, MD

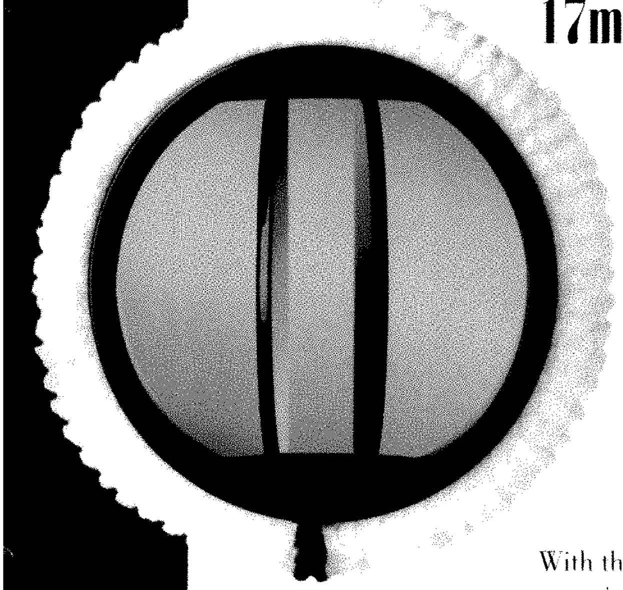
Total Correction of Transposition of Great Arteries With Atrioventricular Septal Defect 989

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Neil Wilson, MRCP, DCH, Zohair Al Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

continued on page A-13

The Hemodynamic Plus Series

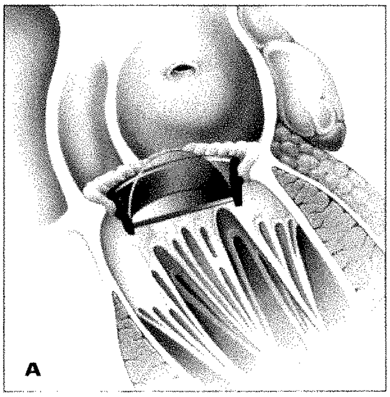
25% more flow area for patients with a 17mm to 21mm annulus



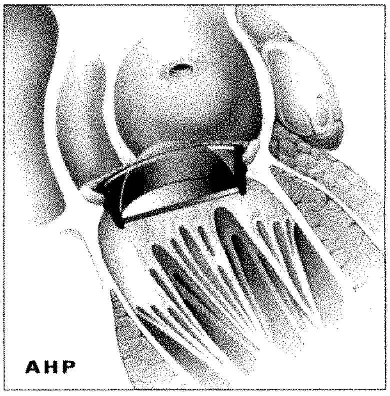
ST. JUDE MEDICAL®
HEART VALVE
HEMODYNAMIC
PLUS SERIES

- ***Proven St. Jude Medical® heart valve design and quality***
- ***Larger orifice area***
- ***Smooth laminar flow for enhanced thromboresistance***
- ***Improved implant position***

With the Hemodynamic Plus (HP) Series valves we took sewing cuff material out of the annulus and added more orifice area.



Standard St. Jude Medical® aortic valve implant position



HP Series valve implant position

The HP Series valves offer you improved hemodynamics for patients with a 17mm to 21mm annulus. For 15 years surgeons and over 450,000 patients have relied on us for the best. Contact your St. Jude Medical, Inc. representative and we'll show you how the best just got better.

Not available in the USA

UNEQUALED PERFORMANCE
15 YEARS
SINCE 1977

ST. JUDE MEDICAL®

Corporate Headquarters
St. Jude Medical, Inc.
One Lillehei Plaza
St. Paul, Minnesota 55117 USA

Customer Service
(612) 483-2000

24-hour Technical/ Professional Consultation
Telephone (800) 328-9634 (USA)
(612) 483-2000
Fax (612) 482-8318

European Headquarters
St. Jude Medical Europe, Inc.
Belgian Branch
Excelsiorlaan 79
1930 Zaventem, Belgium

Customer Service
Telephone 32-2-719-68-11
Telex 20857SJMEUR
Fax 32-2-725-51-62

St. Jude Medical is a registered trademark of St. Jude Medical, Inc.
Refer to the physician's manual provided with each device for detailed instructions for use, warnings, precautions and possible adverse device effects. CAUTION: FEDERAL LAW (USA) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.
Copyright 1992 St. Jude Medical, Inc. All rights reserved. Printed in the USA. WW099220040EN

Announcing research opportunities in blood conservation

Two $25,000 grants supported by Miles Inc.

1. Clinical research in blood conservation in thoracic surgery:	$25,000
2. Clinical research in blood conservation in cardiovascular anesthesia:	$25,000

Grant Information

☐ Both grants are provided by Miles Inc., Pharmaceutical Division; selection is by an independent, highly-qualified selection committee

☐ Eligibility is limited to physicians who have been in academic staff positions for no more than four years

☐ No more than 25% of the grant is to be used by the physicians' institution for indirect costs

☐ Clinical research resulting from the grant will be submitted for publication by the physician

Grant deadline:
March 15, 1993

Grant Announcement by
May 15, 1993

To request application:
Call Bruce Leeb & Company
(201) 612-8919

MILES

Pharmaceutical Division

Printed in USA 1992

Grant Selection

☐ The grant selection committee is chaired by

Michael N. D'Ambra, M.D.
Director, Cardiac Anesthesia Group
Massachusetts General Hospital
Boston, Massachusetts

☐ Dr. D'Ambra is joined in the selection of the grantees by

Leonard L. Firestone, M.D.
Chief of Cardiac Anesthesia
University of Pittsburgh
Pittsburgh, Pennsylvania

Christina T. Mora, M.D.
Assistant Professor of Anesthesiology
Emory University School of Medicine
Atlanta, Georgia

Hartzell V. Schaff, M.D.
Consultant, Cardiovascular Surgery
Professor of Surgery
Mayo Clinic
Rochester, Minnesota

Craig R. Smith, M.D.
Director of Cardiopulmonary Transplant Program
Columbia Presbyterian Medical Center
Associate Professor Clinical Surgery, College of Physicians and Surgeons of Columbia University
New York, New York

Peter K. Smith, M.D.
Assistant Professor of Surgery
Assistant Professor of Biomedical Engineering
Duke University Medical Center
Durham, North Carolina

Continued from page A-10

How to Do It

New Surgical Technique for Total-Defect Aortopulmonary Window 991

Osamu Matsuki, MD, Toshikatsu Yagihara, MD, Fumio Yamamoto, MD, Kyoichi Nishigaki, MD, Hideki Uemura, MD, and Yasunaru Kawashima, MD

Newly Developed Holder for a Right-Angled Metal Venous Cannula 993

Takashi Watanabe, MD, Toshio Abe, MD, Minoru Tanaka, MD, Kenzo Yasuura, MD, Hiroshi Hikosaka, MD, Yoshito Suenaga, MD, and Hidekazu Hosokawa, MD

Modified Urinary Collecting Bags for Prolonged Underwater Chest Drainage 995

Yaron Bar-El, MD, Yair Lieberman, MD, and Alon Yellin, MD

Classics in Thoracic Surgery

Clarence Crafoord and the First Successful Resection of a Cardiac Myxoma 997

W. Randolph Chitwood, Jr, MD

Current Review

Surgical Treatment for Higher Stage Non–Small Cell Lung Cancer 999

Dirk E. Van Raemdonck, MD, Airton Schneider, MD, and Robert J. Ginsberg, MD

Key References

Aortic Valve Repair 1014

Delos M. Cosgrove III, MD

Update

A Method for Predicting Postoperative Lung Function and Its Relation to Postoperative Complications in Patients with Lung Cancer 1016

Kazuya Nakahara, MD, Shinichiro Miyoshi, MD, and Katuhiro Nakagawa, MD

Correspondence

Aprotinin Treatment During Open Heart Operation in a Patient With Severe Thrombocytopenia 1018

Ehud Deviri, MD, Uzi Izhar, MD, Benjamin Drenger, MD, Yitzhak Glick, MD, and Joseph B. Borman, FRCS(Eng)

Thermo Cardiosystems Left Ventricular Assist Device 1019

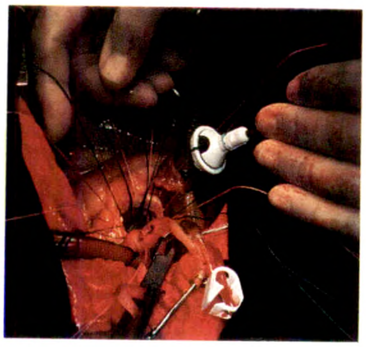
O. H. Frazier, MD

Reply

Nelson A. Burton, MD, W. Stephen Phillips, MD, Quentin Macmanus, MD, and Edward A. Lefrak, MD

continued on page A-15

We call it Hemaflex.™ You'll call it standard operating procedure.



Introducing Hemaflex. It's the new, pure collagen hemostat from the makers of Avitene®(MCH). If you perform cardiovascular or cardiothoracic surgery, Hemaflex should be a part of your standard operating procedure.

•When wrapped around a vessel, Hemaflex has not been reported to have a stenotic effect, unlike other topical hemostatic agents.

•Hemaflex is effective in treating bone and soft tissue sites such as sternotomies and synthetic graft anastomoses.

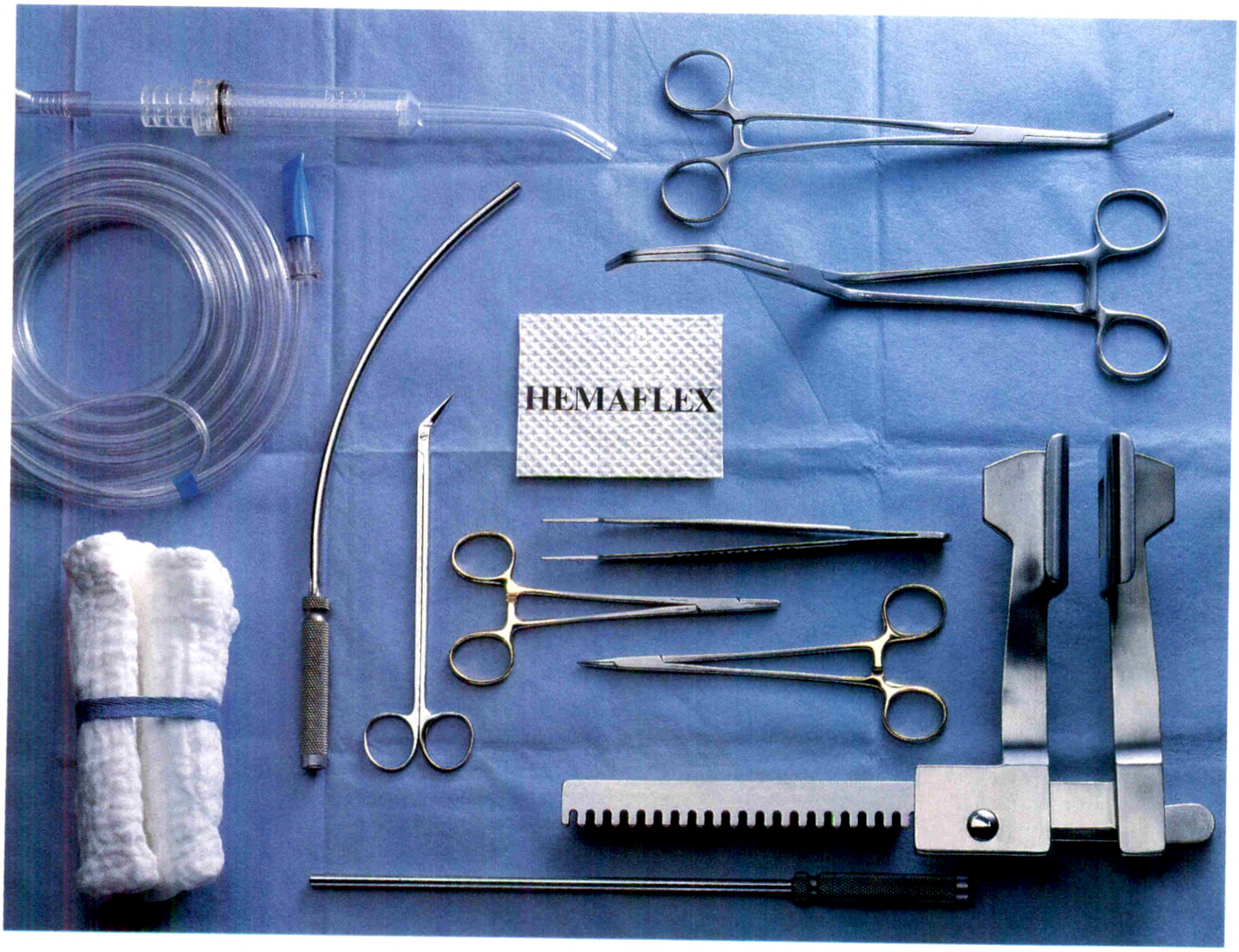
•Hemaflex stops bleeding fast, unlike mechanical barriers, because it is pure collagen. It triggers the body's own blood-clotting response and is absorbed easily.

•Anticoagulation treatment does not interfere with the potent actions of Hemaflex.

•Hemaflex is easy to handle and flexible enough to wrap around vessels.

So find out for yourself why we believe Hemaflex is the ideal choice for cardiovascular and cardiothoracic procedures. Call us today at **1-800-451-4716** (in Mass., **617-938-9328**), and ask for your free sample.

HEMAFLEX™
FROM THE MAKERS OF AVITENE®



Continued from page A-13

Plateletpheresis and Transfusion Practice in Heart Operations 1020

Gerald G. Davies, FFARCSI, Douglas G. Wells, FFARACS, Richard Sadler, MD,
Thomas M. Mabee, MD, Mitchell Ruffcorn, MD, and John B. Dooley, MD

Preoperative Morphologic and Physiologic Assessment of Internal Thoracic Arteries 1020

Charles C. Canver, MD

Reply

Frederick L. Grover, MD

Manual Versus Stapled Bronchial Closure: Still Controversial 1021

Rafael Aguilo, MD, and Miguel Llobera, MD, PhD

Reply

L. Penfield Faber, MD, S. Russell Vester, MD, C. Frederick Kittle, MD,
William H. Warren, MD, and Robert J. Jensik, MD

High-Dose Aprotinin in Emergency Coronary Artery Bypass After Thrombolysis 1022

Franco Alajmo, MD, and Giancarlo Calamai, MD

Reply

Theodore Efstratiadis, MD, PhD, Christopher Munsch, ChM, David Crossman, MB,
and Kenneth M. Taylor, MD

Hemodynamic Effects of Pericardial Closure 1023

Arkalgud Sampathkumar, MD

Reply

Steven Hunter, FRCS, and Gianni D. Angelini, MD

Abrupt Cardiac Failure Using a Right VAD in the Presence of a Tricuspid Valve Prosthesis 1023

Steven C. Griffin, FRCS, and John H. Dark, FRCS

Review of Recent Books

A Textbook of Cardioplegia for Difficult Clinical Problems, edited by Richard M. Engelman, MD, and Sidney Levitsky, MD 994

Edward Y. Sako, MD, PhD

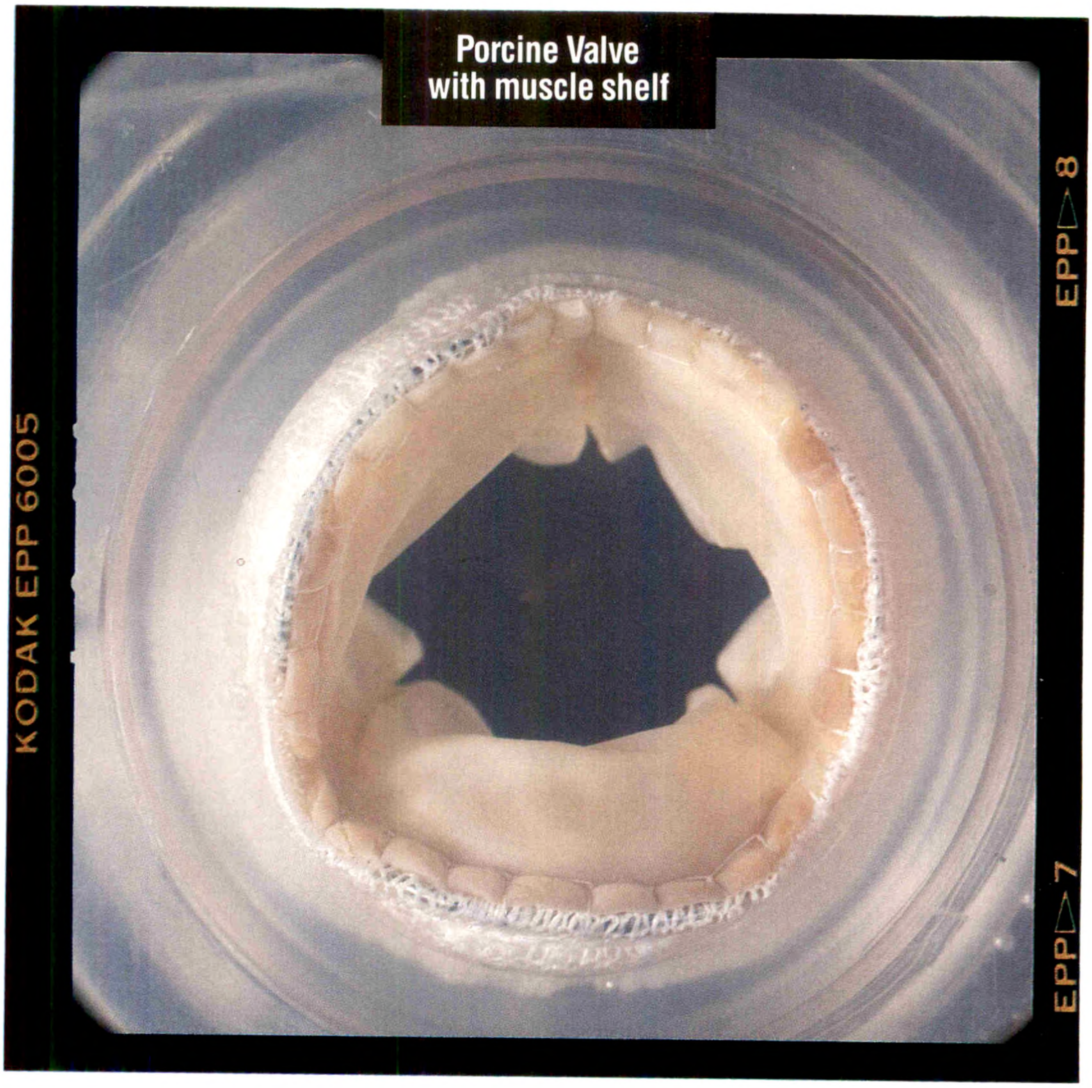
Cardiac and Noncardiac Complications of Open Heart Surgery: Prevention, Diagnosis and Treatment, edited by Morris N. Kotler, MD, and Anthony Alfieri, DO 1015

James L. Nielsen, MD

Announcements

Information for Authors A-25, 26

continued on page A-18



An open and shut case

You can see the difference with the naked eye. The Hancock M.O. Bioprosthesis eliminates the flow-impeding septal muscle shelf of the right coronary cusp and replaces it with a noncoronary cusp from a second, larger valve. With three fully flexible leaflets, the Hancock M.O. valve opens more completely and symmetrically during systole compared with other porcine bioprostheses. Thus, it offers minimal obstruction to blood flow and superior hemodynamics.

This composite design, proven in over 12 years of clinical use, provides excellent hemodynamics in the aortic position. A recent study published in *Circulation* demonstrated that smaller (size 19 and 21mm) Hancock M.O. Bioprostheses

UC 900 3085 EN
Copyright © 1991 by Medtronic, Inc.
1703-7035

for the modified orifice.

have lower gradients and larger valve areas than comparably sized porcine valves retaining the muscle shelf.[1]

Excellent flow characteristics combined with long-term clinical experience make the Hancock M.O. Bioprosthesis the tissue valve of choice for the small aortic root.

For detailed information describing intended use, warnings, precautions, and contraindications, refer to the Instructions For Use provided with the product or contact your local Medtronic representative.

CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician.

Reference: 1. Kahn SS, Mitchell RS, Derby GC, Oyer PE, Miller DC. Differences in Hancock and Carpentier-Edwards Porcine Xenograft Aortic Valve Hemodynamics: Effect of Valve Size. *Circulation.* 1990; 82(suppl 4):117-124.

HANCOCK® M.O.
Modified Orifice Bioprosthesis

Medtronic Heart Valves
Medtronic, Inc.
7000 Central Avenue, N.E.
Minneapolis, MN 55432
Physician's Information Service
(800) 328-2518

Medtronic

Continued from page A-15

Guidelines for the Submission of Electronic Manuscripts A-27

Events of Interest A-28, 29

Forthcoming Articles A-30

Notice From The Society of Thoracic Surgeons 860

Notice From the American Board of Thoracic Surgery 946, 982

Classified Advertisements A-31, 32, 33

Index to Advertisers A-40

GENERAL INFORMATION *The Annals of Thoracic Surgery* is indexed/abstracted in *Index Medicus, Current Contents/Clinical Practice/Life Sciences, Excerpta Medica, Reference Update,* and *Biological Abstracts.*

Please direct orders for subscriptions, single copies, and back issues; changes of address; and claims for missing issues to: Journals Fulfillment Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Claims for missing issues can be honored only up to 3 months for domestic addresses, 6 months for foreign addresses. Duplicate copies will not be sent to replace ones undelivered through failure to notify Elsevier of change of address.

The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery,* Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.

Microfilm copies are available through University Microfilms International, 300 North Zeeb Road, Ann Arbor, MI 48106.

Reprints, except special orders of 100 or more, are available from the authors.

Advertising inquiries should be addressed to: Art Carlucci, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3880).

The publisher assumes no responsibility for any injury and/or damage to persons or property as a matter of products liability, negligence, or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. No suggested test or procedure should be carried out unless, in the reader's judgment, its risk is justified. Because of rapid advances in the medical sciences, we recommend that the independent verification of diagnoses and drug dosages should be made. Discussions, views, and recommendations as to medical procedures, choice of drugs, and drug dosages are the responsibility of the authors.

Although all advertising material is expected to conform to ethical (medical) standards, inclusion in this publication does not constitute a guarantee or endorsement of the quality or value of such product or of the claim made of it by its manufacturer.

This journal has been registered with the Copyright Clearance Center, Inc. Consent is given for the copying of articles for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition that the copier pay through the Center the per copy fee stated in the code on the first page of each article for copying beyond that permitted by the US Copyright Law. The appropriate fee should be forwarded with a copy of the first page of the article to the Copyright Clearance Center, Inc, 27 Congress Street, Salem, MA 01970. If no code appears on an article, the author has not given broad consent to copy, and permission to copy must be obtained directly from the author. This consent does not extend to other kinds of copying, such as for general distribution, resale, advertising and promotional purposes, or for creating new collective works. All inquiries regarding copyrighted material from this publication, other than reproduction through the Copyright Clearance Center, should be directed to Rights and Permissions Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; (212) 633-3977.

This journal is printed on acid-free paper.

© 1992 by The Society of Thoracic Surgeons

13th Annual

SAN DIEGO CARDIOTHORACIC SURGERY SYMPOSIUM

San Diego Marriott Hotel & Marina, February 11 - 14, 1993

Pathophysiology & Techniques of Cardiopulmonary Bypass

Program Director:
Joe R. Utley, M.D.

This course is of interest to all members of the team caring for the cardiac surgery patient, including physicians and surgeons, perfusionists, nurses and nurse anesthesiologists, intensivists, and biomedical health professionals. Continuing education credit will be awarded to physicians, perfusionists, nurses, and CRNAS.

Faculty Includes:
- *James A. Alexander, M.D.*
- *Roy E. Bolles, C.C.P.*
- *Mark E. Bruley, B.S.*
- *John F. Butterworth, IV, M.D.*
- *David A. Cross, M.D.*
- *Richard F. Davis, M.D.*
- *William Edelman*
- *John Fung, M.D.*
- *Glenn P. Gravlee, M.D.*
- *Steven R. Gundry, MD.*
- *Carl C. Hug, Jr., M.D., Ph.D.*
- *W.J. Kolff, M.D.*
- *Glen W. Laub, M.D.*
- *William B. Long, M.D.*
- *George J. Magovern, Jr., M.D.*
- *Jack Marlotte*
- *Dr. Philippe Menacshe*
- *Kathleen S. Music, R.N., J.D.*
- *Luis Oppenheimer, M.D.*
- *Donovan Peterson*
- *A. Thomas Pezzella, M.D.*
- *Albert J. Pfister, M.D.*
- *Robert E. Rawitscher, M.D.*
- *Jeffrey Riley, B.A.*
- *Richard M. Satava, M.D.*
- *Phil Scott, C.C.P.*
- *George Silvay, M.D., Ph.D.*
- *Julie A. Swain, M.D.*
- *Michael S. Sweeney, M.D.*
- *Joseph T. Walls, M.D.*
- *Andrew S. Wechsler, M.D.*
- *Allen Willner, Ph.D.*
- *Prof. Dr. Ch. R.H. Wildevuur, M.D., Ph.D.*
- *Mary Winkler, R.N., C.C.P.*

The symposium will be conducetd in English with simultaneous translations to German & French.

Sponsored by: Cardiothoracic Research & Education Foundation
Co-Sponsored by: World Assoc. of Cardiac, Thoracic & Vascular Anesthesia

Abstracts will be accepted for presentation until January 1, 1993. For abstract forms or program information including registration and hotel accommodation forms, send a postcard with your name, specialty, and address to:

C.R.E.F. P.O. Box 23220, San Diego, CA 92193 or Fax (619) 541-1447 Voice (619) 541-1444

THE MOUNT SINAI MEDICAL CENTER, NEW YORK • Program Director: Randall B. Griepp, M.D.

AORTIC SURGERY SYMPOSIUM III

VIDEO PROCEEDINGS (INCLUDING PANEL DISCUSSIONS)

FACULTY

Jean Bachet, M.D.	Joseph Coselli, M.D.	Nicholas Kouchoukos, M.D.
Hans Borst, M.D.	Joseph N. Cunningham, M.D.	Steven Lansman, M.D.
Christian Cabrol, M.D.	Arisan M. Ergin, M.D.	Kenneth Mattox, M.D.
Alain Carpentier, M.D., Ph.D.	Richard Gorlin, M.D.	D. Craig Miller, M.D.
Denton Cooley, M.D.	Randall Griepp, M.D.	

Aortic Surgery Symposium IV, April 22-23, 1994, New York, New York

PLEASE CHECK

☐ Session I	$ 100
☐ Session II	$ 100
☐ Session III	$ 100
☐ Session IV	$ 100
☐ All four sessions (save $50)	$ 350
* Plus shipping & handling	
U.S. - Ground	$ 15
Canada - Ground	$ 20
Europe - Air	$ 75
State Sales Tax (CA only)	$___
Total Order	$___

ALL FEES IN U.S. DOLLARS DRAWN ON U.S. BANKS
All tapes in NTSE format

☐ Check enclosed ☐ VISA/MasterCard ☐ AmEx

Credit Card #____________________

Expiration Date ____________________

AORTIC SURGERY SYMPOSIUM III • VIDEO ORDER FORM

I agree not to reproduce these videos outside my institute or present this material without prior written permission from Dr. Lansman.

Signature____________________ Date ________

PLEASE PRINT OR TYPE

Name:
First Last M.D., Prof., R.N.

Shipping Address

City State Zip Country

Telephone Fax

Signature for Credit Card

Mail to: PROMEDICA INTERNATIONAL • 620 Newport Center Drive, Suite 575 • Newport Beach, CA 92660 • USA
Contact: Lisa Turnbull • TEL (714) 640-5870 Ext 20 • FAX (714) 759-6911

NATIONAL UNIVERSITY OF SINGAPORE
DEPARTMENT OF SURGERY

Applications are invited for teaching appointments in the Department of Surgery. Candidates should possess an approved basic medical degree. In addition, he/she must possess one of the following: Board certificate in cardiothoracic surgery, FRCS or equivalent with experience in cardiothoracic surgery.

Candidates applying for the position of Senior Lecturer or Associate Professor must be adequately experienced in the full range of cardiothoracic surgery, including surgical management of paediatric cardiothoracic problems, acquired valvular diseases and coronary artery disease. The candidate is expected to be experienced in thoracic vascular problems. The Department also deals with thoracic surgery.

There are opportunities for active clinical practice in open heart, thoracic and vascular surgery with experimental surgical research and undergraduate and postgraduate teaching.

Gross annual emoluments range as follows:

Lecturer	S$53,160 - 64,200
Senior Lecturer	S$58,680 - 100,310
Associate Professor	S$88,650 - 122,870

(US$1.00 = S$1.59 approximately)

The commencing salary will depend on the candidate's qualifications, experience and the level of appointment offered. In addition, appointees who are on regular appointments will receive a Specialist Allowance (SA) under the Professional Fee Scheme, the rates for which are as follows:

Lecturer	15% or 20% of gross salary
Senior Lecturer	25% or 40% of gross salary
Associate Professor	40% of gross salary

Senior Lecturers and Associate Professors who are designated Consultants may retain in full professional fees earned during the clinical sessions devoted to private patients which are over and above their SA up to twice their gross annual salary. For additional fees earned thereafter, part of the fees to be retained by the staff member will depend on his contribution to teaching, research and clinical service. Lecturers and Senior Lecturers designated as Senior Registrars may retain professional fees earned over and above their SA, up to 60% of their gross annual salary. The number of sessions for private patients will be limited to 4 out of 11 sessions in a week.

Staff on visiting appointments will be provided with emoluments comparable to those offered to staff on regular contracts.

Leave and medical benefits will be provided. Depending on the type of contract offered, other benefits may include: provident fund benefits or an end-of-contract gratuity, a settling-in allowance of S$1,000 or S$2,000, subsidised housing at nominal rentals ranging from S$100 to S$216 p.m., education allowance for up to three children subject to a maximum of S$16,425 per annum per child, passage assistance and baggage allowance for the transportation of personal effects to Singapore.

Application forms and further information on terms and conditions of service, including the Professional Fee Scheme, may be obtained from:

The Director
Personnel Department
National University of Singapore
10 Kent Ridge Crescent
Singapore 0511

The Director
North America Office
National University of Singapore
55 East 59th Street
New York, NY 10022, USA
Tel: (212) 751-0331

Enquiries may also be sent through **BITNET** to: **PERSDEPT @ NUSVM**, or through **Telefax: (65) 7783948**

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Editor

Thomas B. Ferguson, MD, St. Louis, MO

Herbert Sloan, MD, Editor 1969–1984
John D. Steele, MD, Editor 1964–1969

Associate Editors

John R. Benfield, MD, Sacramento, CA

Anthony R. C. Dobell, MD, Montreal, Canada

Marvin M. Kirsh, MD, Ann Arbor, MI

Hassan Najafi, MD, Chicago, IL

J. Kent Trinkle, MD, Book Review Editor
University of Texas Health Science Center
7703 Floyd Curl Drive, San Antonio, TX 78284-7841

Editorial Board

Hendrick B. Barner, MD, New Hyde Park, NY
Harvey W. Bender, Jr, MD, Nashville, TN
Ray Chu-Jeng Chiu, MD, PhD, Montreal, Canada
Lawrence H. Cohn, MD, Boston, MA
Jack G. Copeland III, MD, Tucson, AZ
Delos M. Cosgrove III, MD, Cleveland, OH
Timothy J. Gardner, MD, Baltimore, MD
William A. Gay, Jr, MD, Salt Lake City, UT
Robert A. Guyton, MD, Atlanta, GA
Clement A. Hiebert, MD, Windham, ME
Takashi Iwa, MD, Kanazawa, Japan
Robert B. Karp, MD, Chicago, IL
James E. Lowe, MD, Durham, NC
Douglas J. Mathisen, MD, Boston, MA
Philippe Menasché, MD, PhD, Paris, France
William I. Norwood, Jr, MD, Philadelphia, PA
John L. Ochsner, MD, New Orleans, LA
Mark B. Orringer, MD, Ann Arbor, MI
Peter C. Pairolero, MD, Rochester, MN
Richard M. Peters, MD, Palo Alto, CA
W. Gerald Rainer, MD, Denver, CO
Charles L. Roper, MD, St. Louis, MO
Thomas W. Shields, MD, Chicago, IL
Jaroslav Stark, MD, London, England
Larry W. Stephenson, MD, Detroit, MI
Kenneth M. Taylor, MD, London, England

Administrative Editor

Carol L. Blasberg, St. Louis, MO

Editorial Office

The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

To provide a place for ALL thoracic surgeons to relate experiences which will help other practicing thoracic surgeons give better patient care.
Herbert Sloan, MD

AVAILABLE NOW ON VIDEOTAPE

TECHNIQUES IN
CONGENITAL CARDIAC SURGERY
at Children's Hospital
Boston, Massachusetts

Aldo R. Castaneda, M.D.
Frank L. Hanley, M.D.
Richard A. Jonas, M.D.
John E. Mayer, M.D.

Video Library - Volume 2

- FENESTRATED FONTAN PROCEDURE
- SINGLE PERICARDIAL PATCH REPAIR OF COMPLETE AV CANAL
- ALLOGRAFT REPAIR OF TETRALOGY OF FALLOT WITH PULMONARY ATRESIA

This videocassette provides a comprehensive intraoperative demonstration of techniques currently employed at The Children's Hospital, Boston, in the repair of complex single ventricle, complete AV canal and tetralogy with pulmonary atresia. Professional video photography, illustration and editing has insured outstanding clarity and detail. Available in VHS, Beta and 3/4" in all international formats.

PRICE: $250

Please send me **Techniques in Congenital Cardiac Surgery - Volume 2** for $250 (U.S.) plus $5 for shipping and insurance within the U.S. and $10 for shipping and insurance outside the U.S.

SIZE: ☐ VHS ☐ Beta ☐ 3/4" U-Matic

FORMAT: ☐ NTSC (USA, Canada, Japan, S. America)
☐ PAL (Europe, Asia, Australia, S. America)
☐ SECAM (CIS, Mid East, E. Europe, France)

☐ Make **CHECK** or **MONEY ORDER** payable to:
Surgical Techniques Video

☐ **CHARGE TO:** ☐ MasterCard ☐ Visa ☐ American Express
Card Number ____________________
Expiration Date ________ Signature ____________

☐ Send information on Volume I in this series.

Quantity ______ @ $250 each = $ ________
Shipping within U.S. @ $5 each = $ ________
outside U.S. @ $10 each = $ ________
TOTAL ENCLOSED (U.S. dollars) $ ________

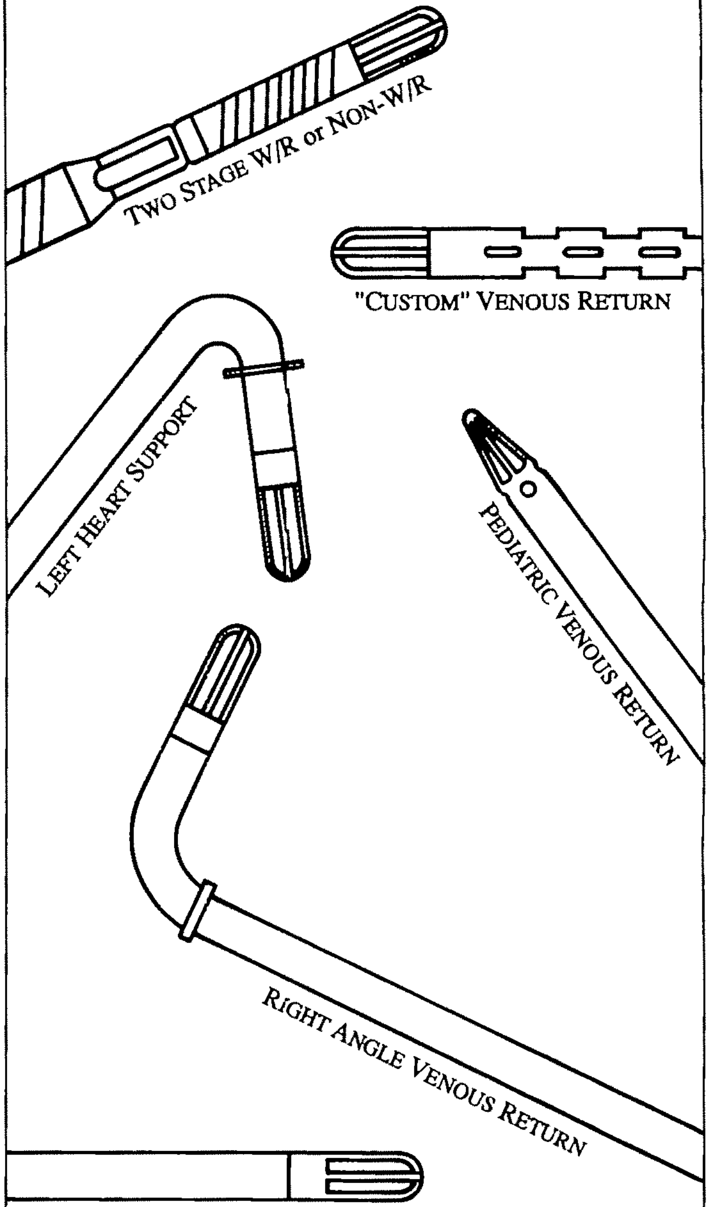
Name ____________________
Organization ____________________
Street Address ____________________
City ____________ State/Province ________
Zip/Postal Code ________ Country ________
Telephone ________ Fax ________

Return to:
WEISMAN VIDEO PRODUCTIONS
50 Hunt Street
Watertown, Massachusetts 02172-4625
U.S.A.

TEL: 617.926.2089 FAX: 617.926.7965

Outside USA please pay by money order in US dollar equivalent or use credit card.
Prices subject to change.
For more personalized service, please contact
Weisman Video Productions at address above.

IT'S THE
POLYSTAN TIP
THAT COUNTS



WHEN DISCUSSING
VENOUS RETURN CAPABILITIES

Vitalcor/ POLYSTAN

Vitalcor Inc.
100 E. Chestnut Ave.
Westmont, Illinois 60559
(708) 323-3888 Fax: (708) 325-0257
Call Toll-Free: 1-800-874-8358

Quality
Without
Compromise

"Vitalcor, Inc. is the exclusive distributor of Polystan products in the USA"

The Society of Thoracic Surgeons

Officers

President	Vincent L. Gott, MD
Vice President	Denton A. Cooley, MD
Secretary	Richard P. Anderson, MD
Treasurer	Nicholas T. Kouchoukos, MD
Editor	Thomas B. Ferguson, MD
Historian	W. Gerald Rainer, MD

Councillors at Large

Leonard L. Bailey, MD
James L. Cox, MD
H. Storm Floten, MD
Timothy J. Gardner, MD
Robert J. Ginsberg, MD
Peter C. Pairolero, MD

Business Manager
Walter G. Purcell

Southern Thoracic Surgical Association

Officers

President	William A. Cook, MD
President-Elect	Gordon F. Murray, MD
Vice President	Joseph I. Miller, Jr, MD
Secretary-Treasurer	Hendrick B. Barner, MD
Editor	Thomas B. Ferguson, MD
Historian	Hawley H. Seiler, MD

Council

Robert M. Sade, MD
Chairman
William C. Alford, Jr, MD
Hendrick B. Barner, MD
William A. Cook, MD
Timothy J. Gardner, MD
Joseph I. Miller, Jr, MD
Gordon F. Murray, MD
D. Glenn Pennington, MD
William F. Sasser, MD
Thomas B. Ferguson, MD (Ex Officio)

Business Manager
Walter G. Purcell

For information about either organization, contact either The Society of Thoracic Surgeons or the Southern Thoracic Surgical Association at 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610 (facsimile: (312) 527-6635).

The Annals of Thoracic Surgery

Affix mailing label here.

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC

Elsevier Science Publishing Co., Inc.
Attn: Journal Customer Service Department
P.O. Box 882, Madison Square Station
New York, New York 10159
Telephone # (212) 633-3950

☐ **Moving?** Please give us 6 weeks advance notice. Attach your old label here for better service. Print your new address and zip code below.

☐ **Entering a New Subscription?** Please fill out the order form below.

☐ **A Problem or Query?** We can serve you best if you include your mailing label with any correspondence.

Name ____________________
Address ____________________
____
City/State ____________________
Country/Zip Postal Code ____________________
Specialty ____________________

I am a member of:
☐ The Society of Thoracic Surgeons
☐ The Southern Thoracic Surgical Association
☐ both

New Subscriptions
☐ Please enter my 1992 subscription to **The Annals of Thoracic Surgery**, ISSN 0003-4975, Volumes 53, 54 (12 issues)
☐ Institutional rate: $165.00
☐ Personal rate: $95.00*

Postage and Handling: For air delivery in the U.S., Canada and Mexico, add $80.00. Subscribers outside the U.S. must add one of the following postal options: $35.00 for surface delivery; $70.00 for surface air lift delivery to Europe; $85.00 for surface air lift delivery to Japan; or $160.00 for air delivery to the rest of the world.

Enclosed is my: ☐ personal check ☐ bank draft
Charge to: ☐ American Express ☐ VISA
☐ MasterCard (issuing bank # __________)

Account # ____________________ Expires __________

Signature ____________________

☐ Please bill me (Orders from non-U.S. customers must be prepaid.)

Note: Personal subscriptions begin with the first month after processing of your order unless otherwise indicated. Journal rates valid through December 31, 1992.

*The personal rate is available to individuals only at home address or medical institutions.

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC

9/91 XIGA

MAYO CLINIC

Mayo Clinic is seeking a thoracic and cardiovascular surgeon to join their group medical practice in Jacksonville, Florida. Candidates should be eligible for or certified by the American Board of Thoracic Surgery or the equivalent if trained abroad. Clinical expertise in general thoracic and adult cardiac surgery is required. Position has academic appointment appropriate for surgeon's qualifications. Forward curriculum vitae and name/addresses of three references to:

Peter C. Pairolero, MD, Chair
Division of Thoracic &
Cardiovascular Surgery
Mayo Clinic
200 First Street Southwest
Rochester, MN 55905

Mayo Foundation is an affirmative action and equal opportunity educator and employer.

THE ANNALS OF THORACIC SURGERY
INFORMATION FOR AUTHORS

Thomas B. Ferguson, MD
Editor, *The Annals of Thoracic Surgery*
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

The Annals of Thoracic Surgery publishes original papers on topics in thoracic and cardiovascular surgery. Also featured are case reports, "how to do it" articles, classics in thoracic surgery, collective and current reviews, correspondence, and book reviews. All manuscripts, correspondence, and editorial business should be sent to the above address. Guidelines for collective and current reviews are available on request.

If a manuscript is accepted for publication, certain conditions must be agreed to by all authors. These include statements regarding conflict of interest, scientific responsibility, exclusive publication, and assignment of copyright. Elsevier Science Publishing Co, Inc, will maintain records of copyright for The Society. No part of the published material may be reproduced elsewhere without written permission from the publisher.

Because of escalating postage costs, manuscripts and illustrations will not routinely be returned to the authors. The editorial office will be responsible for proper disposal of the manuscripts so that confidentiality is preserved. Manuscripts and illustrations will be returned only if requested and a self-addressed stamped (US postage) envelope provided.

Checklist

The following checklist is provided for the author's convenience. Please utilize this list to make certain the manuscript is complete when submitted. Incomplete manuscripts cannot be accepted for editorial review.

General

- ☐ Submit original and *two* duplicate manuscripts (including three clearly separated and labeled sets of illustrations). Retain a fourth complete set as insurance against loss in the mail.
- ☐ Type manuscript double-spaced throughout (including title page, abstract, text, references, tables, and legends) on one side only on 22 × 28 cm (8½ × 11 inch) opaque bond paper with 3 cm (1¼ inch) margins all around. *This also applies to correspondence.* Type the last name of the first author in the upper right-hand corner of each page, including the title page.
- ☐ Arrange manuscript as follows: (1) title page, (2) abstract, (3) text, (4) references, (5) tables, and (6) legends. Number pages consecutively, beginning with the title page as page 1 and ending with the legend page.
- ☐ A manuscript for an *original article* ordinarily should not exceed 26 double-spaced typewritten pages, and should be proportionally shorter the more illustrations and tables that are included.
- ☐ The *text* for case reports should be *no more* than 4 double-spaced typewritten pages. If tables or illustrations are included, the text must be reduced. The text for a "how to do it" article should be even briefer, but with detailed illustrative material. Case reports and "how to do it" articles that exceed the allowable length will not be considered for publication.
- ☐ Referencing should be selective and pertain directly to the work being reported. Except in collective and current reviews, comprehensive listings serve no useful purpose and utilize valuable space. As a general guide, original articles should have no more than 20 references; case reports, 8 references; and "how to do it" articles, 5 references.

Title Page

- ☐ Give the paper as short a title as possible. Also submit a short title of 3 or 4 words to be used as a running head. Include only the names of the authors directly affiliated with the work, stating for each the single highest academic degree. Include the name and location of no more than two institutional affiliations.
- ☐ If the paper has been or is to be presented at the annual meeting of The Society of Thoracic Surgeons, the Southern Thoracic Surgical Association, or another scientific organization, provide a footnote giving the name, location, and dates of the meeting.
- ☐ At the bottom of the page, type "Address reprint requests to Dr . . ." followed by the last name, exact postal address with zip code, *telephone number, and FAX number* of the author to whom communications, proofs, and requests for reprints should be sent.

Abstracts

- ☐ Provide an abstract *no longer than 175 words* for an original article. Abstracts for case reports and "how to do it" articles should be shorter (50 to 75 words). An abstract must accompany *every* contribution, except for letters to the editor. Include several (3 to 5) keywords to assist in cross-indexing the article.

Text

- ☐ Generally, the text should be organized as follows: Introduction, Material and Methods, Results, and Comment.
- ☐ *Cite references, illustrations, and tables in numerical order* in the text. (Order of mention in text determines the number given to each.)
- ☐ Spell out, or define in parentheses, all abbreviations, even if they are commonly employed.
- ☐ Give all measurements and weights in *Système International (SI) units.* See "SI Unit Implementation—the Next Step" (JAMA 1988;260:73–6).
- ☐ For statistical nomenclature and data analysis, follow the "Guidelines for Data Reporting and Nomenclature" published in *The Annals of Thoracic Surgery* (1988;46:260–1) and found in the program book for the annual meeting of The Society of Thoracic Surgeons.
- ☐ Type footnotes at the bottom of the manuscript page on which they are cited. Credit suppliers of drugs, equipment, and other material described at length in the paper in footnotes, giving company name and location.
- ☐ Type acknowledgments, including complete grant or subsidy information, at the end of the text before the references.

References

- ☐ Identify references in the text using arabic numerals in parentheses on the line. Do not cite personal communications, manuscripts in preparation, and other unpublished data in the reference list. They may be mentioned in the text in parentheses.
- ☐ Type references double-spaced on a separate sheet. *Number consecutively in the order in which they are mentioned in the text.*
- ☐ Journal references should provide *inclusive* page numbers; book references should cite *specific* page numbers.
- ☐ Double-check references for accuracy, completeness, and nonduplication.

(Continued)

© 1992 by The Society of Thoracic Surgeons

☐ Abbreviations of journals should conform to those used in *Index Medicus*. The style and punctuation of the references should follow the formats outlined below:

Journal Article

8. Grillo HC, Suen HC, Mathisen DJ, Wain JC. Resectional management of thyroid carcinoma invading the airway. Ann Thorac Surg 1992;54:3–10.

(List *all* authors if 6 or fewer; otherwise list first 3 and add "et al.")

Chapter in Book

12. Vouhé PR. Transplantation of thoracic organs in children. In: Fallis JC, Filler RM, Lemoine G, eds. Pediatric thoracic surgery. New York: Elsevier, 1991:319–29.

Book (Personal Authors or Editors)

18. Shields TW, ed. Mediastinal surgery. Philadelphia: Lea & Febiger, 1991:1–10.

Tables

☐ Tables should be typewritten *double-spaced* on separate sheets, each with a table number (arabic) and title above the table and explanatory notes and legends below. Provide a key in alphabetical order to each table to identify all abbreviations used; this key should be placed below any explanatory notes.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published table(s).

☐ Tables should be self-explanatory, and the data should not be duplicated in the text or illustrations. If a table provides redundant information, it will be deleted.

Legends

☐ Type legends double-spaced on a single sheet. Numbers should be arabic and correspond to the order in which the illustrations occur in the text. Identify (in alphabetical order) all abbreviations appearing in the illustrations at the end of each legend. Give the type of stain and magnification power for all photomicrographs.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published illustration(s).

☐ Enclose signed releases for recognizable (unmasked) photographs of human beings.

Illustrations

☐ Submit *triplicate* sets, each set in its own envelope, of *unmounted* and untrimmed black and white professionally prepared glossy prints. Components of the same illustration (eg, parts A and B) should be submitted separately. Photographs, rather than original art or photocopies, should be provided. All lettering should be done professionally and should be of adequate size to retain clarity after reduction (*final* lettering size in print should be 1.5 mm high). Illustrations will be reproduced at a width of one column (8.25 cm, 3¼ inches) or two columns (17.15 cm, 6¾ inches), or at an intermediate width ranging from 10.16 to 12.07 cm (4 to 4¾ inches).

☐ Many computer-generated illustrations are unsatisfactory for reproduction and should be professionally redrawn. Roentgenogram reproductions should be no smaller than 13 × 18 cm (5 × 7 inches).

☐ Place the first author's last name, the figure number, and an arrow indicating the *top* on a gummed label on the back of each illustration.

☐ If color illustrations are to be considered for publication, submit *both* positive 35-mm transparencies and color prints. Part of the printing costs for color illustrations will be borne by *The Annals*; however, the author must be prepared to pay $1,150 for the first color illustration on each page and $250 for every additional color illustration on the same page.

Human Investigation

☐ Include the date of approval by the local institutional human research committee or the ethical guidelines that were followed by the investigators in the Material and Methods section of the manuscript.

Humane Animal Care

☐ The Material and Methods section must contain a statement assuring that all animals have received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

Conflict of Interest

The Annals expects authors to disclose any commercial association that might pose a conflict of interest in connection with this manuscript. All funding sources supporting the work should be acknowledged in a footnote. Institutional or corporate affiliations of the authors that might constitute a conflict should be brought to the attention of the Editor.

Scientific Responsibility Statement

Before publication of an accepted manuscript, each author will be required to certify that he or she has participated sufficiently in the work to take responsibility for a meaningful share of the content of the manuscript, and that this participation included:

(a) conception or design of the experiment(s), or collection and analysis or interpretation of data;

(b) drafting the manuscript or revising its intellectual content; and

(c) approval of the final version of the manuscript to be published.

Exclusive Publication Statement

I certify that none of the material in this manuscript has been published previously, and that none of this material is currently under consideration for publication elsewhere. This includes symposia, transactions, books, articles published by invitation, and preliminary publications of any kind except an abstract of 400 words or fewer.

____

(Author's Signature)

Guidelines for the Submission of Electronic Manuscripts

☐ Please note that only the final accepted revision of a manuscript should be submitted as an electronic file. If you are planning to submit a manuscript in this format, please check box.

I. *Keyboarding of Manuscripts*

1) Our equipment can handle the following programs (any version) in their "native" format:

IBM Compatible

DisplayWrite
Executive Writer
Leading Edge
MicroSoft Word
Multimate
Office Writer
PC Write
PFS: Write
PFS: Professional
Q & A Write
Samna
Spellbinder
Volkswriter
WordPerfect
WordStar
WordStar 2000
Xywrite

Macintosh (do not use "Fast Save")

MacWrite
Microsoft Word
WordPerfect

Other word processors should be saved as ASCII files. For files saved as ASCII, consult the editorial office regarding the keyboarding of attributes such as bold, underline, superscript, subscript, etc.

2) All design considerations for typefaces, page layout, and artwork will be handled by the publisher after receipt of the electronic manuscript. **There is no need for the author to input special typesetting codes.**

3) Be especially sure to distinguish between the letters O and I and the numbers 0 and 1, respectively.

4) A "hard return" results from tapping the keyboard's **Enter** key. Use a hard return only to end a paragraph, or for titles, subheads, separate items on a list, etc. Rely on the word processor's word wrap ("soft return") within paragraphs, list items, etc.

5) Use your word processor's capabilities for the following text attributes:
   a) bold
   b) underline and italic
   c) subscript
   d) superscript
   e) strikeout

Text that will be italic in published form may be keyboarded italic or underlined.

6) **Do not use your word processor's hyphenation capabilities. Do not right justify text. Use two hyphens for long dashes.**

7) **In tables, use only tabs, not spaces, to align columns.**

II. *Organization and Delivery of Electronic Files*

1) Accepted manuscripts may be submitted on 3.5" or 5.25" diskettes, which must be either MS-DOS or Macintosh format. The author should retain copies of all files as backup. All diskettes must be accompanied by the *final* revision and a duplicate copy of the manuscript (including two clearly separated and labeled sets of illustrations) in full conformity with the standard Information for Authors on the preceding pages.

2) Diskettes should each be labeled with:
   a) author's name
   b) short title of article
   c) operating system
   d) format
   e) word processor used, including version number.

For example, DOS/DSDD/WordPerfect 4.2, or MAC/800K/MS Word v.3. Here, *DOS* and *Mac* indicate the operating system, *DSDD* (double-sided, double density) or *800K* indicates the diskette's physical format, and the remainder indicates the word processor used. Labels for your use are available from the Editorial Office.

3) If possible, it is helpful to have additional material such as tables, figure legends, and references saved as individual files—one file for each category. A file key should accompany the diskette.

4) Submit only the final accepted version of a manuscript. It is essential that submitted electronic files exactly match the final printout.

5) Diskettes should be packed between cardboard (or with foam or bubble-wrap) in an envelope that states that magnetic media is contained.

Please submit your word-processing diskette, the final revision and a duplicate copy of your manuscript, and two clearly separated and labeled sets of illustrations to:

Thomas B. Ferguson, MD
Editor
The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041

Telephone: (314) 361-6084
FAX: (314) 367-0585

© 1992 by The Society of Thoracic Surgeons

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

■ Le Club Mitrale, Paris, France—December 7–9, 1992

For information on this live teleconference, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870 (facsimile: (714) 759-6911).

■ Specialty Review in Thoracic Surgery, Chicago, Illinois—January 11–16, 1993

For information on this review, sponsored by The National Center for Advanced Medical Education, contact the Registration Office, 707 S Wood St, Chicago, IL 60612; or call toll-free any time: 1-(800) 621-4651.

■ Introduction to Mitral Valve Surgery, Dallas, Texas—January 21–22, 1993

For information on this live teleconference, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 20 (facsimile: (714) 759-6911).

■ First International Symposium on Thoracoscopic Surgery, San Antonio, Texas—January 22–23, 1993

For information on this meeting, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons, San Antonio, Texas—January 25–27, 1993

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

■ Third World Congress of the International Society of Cardio-Thoracic Surgeons, Salzburg, Austria—January 25–27, 1993

For information on this meeting, contact Prof Dr Felix Unger, c/o Interconvention, Austria Center Vienna, A-1450 Vienna, Austria; or telephone +43/1/23 69-26 43 (facsimile: +43/1/23 69-648).

■ Thirteenth Annual San Diego Cardiothoracic Surgery Symposium, San Diego, California—February 11–14, 1993

For information on this meeting, entitled "Pathophysiology & Techniques of Cardiopulmonary Bypass," contact CREF, PO Box 23220, San Diego, CA 92193; or telephone (619) 541-1444.

■ Forty-second Annual Meeting of the American College of Cardiology, Anaheim, California—March 14–18, 1993

For information on this meeting, contact American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814; or telephone (800) 253-4636.

■ Neurohumoral Effects of Profound Hypothermia in Infant Heart Surgery, London, England—March 18–19, 1993

For information on this meeting, contact The Postgraduate Centre, National Heart and Lung Institute, Dovehouse St, London SW3 6LY, England; or telephone 071-351 8172 (facsimile: 071-376 3442).

■ Le Club Mitrale, Paris, France—March 27–April 3, 1993

For information on this live teleconference, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ One Hundred Thirteenth Annual Meeting of the American Surgical Association, Baltimore, Maryland—April 1–3, 1993

For information on this meeting, contact American Surgical Association, Department of Surgery, CB 7245, University of North Carolina, 136 Burnett-Womack Building, Chapel Hill, NC 27599; or telephone (919) 966-4320 (facsimile: (919) 966-6009).

■ American College of Surgeons, Montreal, Canada—April 25–28, 1993

For information on this meeting, contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050 (facsimile: (312) 440-7014).

■ Seventy-third Annual Meeting of the American Association for Thoracic Surgery, Chicago, Illinois—April 26–28, 1993

For information on this meeting, contact American Association for Thoracic Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Fourteenth Annual Scientific Session of the North American Society of Pacing and Electrophysiology, San Diego, California—May 6–8, 1993

For information on this meeting, contact NASPE, 377 Elliot St, Newton Upper Falls, MA 02164; or telephone (617) 244-7300 (facsimile: (617) 244-3920).

■ 1993 World Symposium on Cardiomyoplasty and Biomechanical Assist, Paris, France—May 24–26, 1993

For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 22 (facsimile: (714) 759-6911).

■ The International Society for Cardiovascular Surgery/The Society for Vascular Surgery, Washington, DC—June 7–9, 1993

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Fifth European Congress on Extra-Corporeal Circulation Technology, Arles, France, June 9–12, 1993

For information on this meeting, contact MOBO Promotions/FECECT, Catharijnesingel 105, 3511 GV Utrecht, Netherlands; or telephone 31-(0)30-310751 (facsimile: 31-(0)30-311198).

■ World Congress on Diseases of the Chest, Amsterdam, the Netherlands—June 13–18, 1993

For information on this meeting, contact XVII World Congress on Diseases of the Chest, International Academy of Chest Physicians & Surgeons, 3300 Dundee Rd, Northbrook, IL 60062-2348.

■ Nineteenth Annual Meeting of The Western Thoracic Surgical Association, Carlsbad, California—June 24–26, 1993

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Le Club Mitrale, Paris, France, June 26–June 3, 1993

For information on this live teleconference, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, ext 28 (facsimile: (714) 759-6911).

■ Twenty-first World Congress of The International Society for Cardiovascular Surgery, Lisbon, Portugal—September 12–15, 1993

For information on this meeting, contact ISCVS XXIst World Congress, Congress Secretariat, 13 Elm St, Manchester, MA 01944.

■ Neurological Injury and Pediatric Cardiac Surgery (including results of the prospective Boston Circulatory Arrest Study), Boston, Massachusetts, September 30–October 2, 1993

For information on this meeting, contact Laura Young, Department of Cardiac Surgery, Children's Hospital, 300 Longwood Ave, Boston, MA 02115; or telephone (617) 735-7930 (facsimile: (617) 735-6742).

■ Fifty-ninth Annual Scientific Assembly, American College of Chest Physicians, Orlando, Florida—October 24–28, 1993

For information on this meeting, contact American College of Chest Physicians, 3300 Dundee Rd, Northbrook, IL 60062; or telephone (708) 498-1400 (facsimile: (708) 498-5460).

■ Sixty-sixth Scientific Session of the American Heart Association, Atlanta, Georgia, November 8–11, 1993

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 373-6300 (facsimile: (214) 373-3406).

FORTHCOMING ARTICLES

Original Articles

■ Aprotinin Therapy for Reoperative Myocardial Revascularization: A Placebo-Controlled Study

Delos M. Cosgrove III, MD, Blaine Heric, MD, Bruce W. Lytle, MD, Paul C. Taylor, MD, Roberto Novoa, MD, Leonard R. Golding, MD, Robert W. Stewart, MD, Patrick M. McCarthy, MD, and Floyd D. Loop, MD

■ Bioassay of EDRF From Internal Mammary Arteries: Implications for Early and Late Bypass Graft Patency

Paul J. Pearson, MD, PhD, Paulo R. B. Evora, MD, PhD, and Hartzell V. Schaff, MD

■ Clinical Cardiomyoplasty: Preoperative Factors Associated With Outcome

Anthony P. Furnary, MD, James A. Magovern, MD, Ignacio Y. Christlieb, MD, Judith E. Orie, MD, Kathleen Simpson, BS, and George J. Magovern, MD

■ Combined Carotid and Coronary Revascularization: The Preferred Approach to the Severe Vasculopath

Robert J. Rizzo, MD, Anthony D. Whittemore, MD, Gregory S. Couper, MD, Magruder C. Donaldson, MD, Sary F. Aranki, MD, John J. Collins, Jr, MD, John A. Mannick, MD, and Lawrence H. Cohn, MD

■ Device-Supported Myocardial Revascularization: Safe Help for Sick Hearts

Michael S. Sweeney, MD, and O. H. Frazier, MD

■ Early Cellular Events in the Lung Allograft

Riad Adoumie, MD, Cyril Serrick, BS, Adel Giaid, PhD, and Hani Shennib, MD

■ Fluosol Cardioplegia Results in Complete Functional Recovery: A Comparison With Blood Cardioplegia

Jeffrey M. Pearl, MD, Hillel Laks, MD, Davis C. Drinkwater, MD, Avedis Meneshian, BS, Steven M. Martin, MD, Mark Curzan, MS, and Paul A. Chang, BS

■ Fontan Procedure for Hypoplastic Left Heart Syndrome

William I. Norwood, Jr, MD, PhD

■ Low-Dose Aprotinin in Internal Mammary Artery Bypass Operations Contributes to Important Blood Saving

Jacques P. A. M. Schönberger, MD, Peter A. M. Everts, EKP, Husam Ercan, MD, Johan J. Bredée, MD, PhD, Johan H. Bavinck, MD, Eric Berreklouw, MD, and Charles R. M. Wildevuur, MD, PhD

■ Mediastinitis in Heart Transplantation

Shreekanth V. Karwande, MD, Dale G. Renlund, MD, Stephanie L. Olsen, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, John A. Hawkins, MD, Roger C. Millar, MD, and John D. Marks, PE

■ Pulmonary "Twinning" Procedure: Use of Lungs From One Donor for Single-Lung Transplantation in Two Recipients

David A. Haydock, MD, Donald E. Low, MD, Elbert P. Trulock, MD, Larry R. Kaiser, MD, Michael K. Pasque, MD, Ernesto Molmenti, MD, and Joel D. Cooper, MD

Case Reports

■ Management of Severe Bronchial Ischemia After Bilateral Sequential Lung Transplantation

Derya Oturanlar, MD, Walter Klepetko, MD, Michael Grimm, MD, Adelheid End, MD, Wilfried Wisser, MD, Thomas Wekerle, MD, and Ernst Wolner, MD

■ Surgical Treatment of Postinfarction Ventricular Septal Defect With Aortic Stenosis

Lauren R. Boglioli, BS, Thomas A. Traill, MRCP, Alfred S. Casale, MD, Bruce A. Reitz, MD, and Duke E. Cameron, MD

How to Do It

■ Inverted Y Incision for Accurate Tailoring of Patches and Vessels

Darryl Hoffman, FRCS, and Robert W. M. Frater, FRCS

■ Repairing the Degenerative Anterior Mitral Leaflet

John M. Alvarez, FRACS, Narcissus Teoh, MB, BS, and Cedric W. Deal, FRACS

Classics in Thoracic Surgery

■ The Nissen Fundoplication

F. Henry Ellis, Jr, MD, PhD

Current Review

■ Release of Vasoactive Substances During Cardiopulmonary Bypass

Stephen W. Downing, MD, and L. Henry Edmunds, Jr, MD

Allogenic Vein as a Conduit for Coronary Artery Bypass

Hendrick B. Barner, MD

Division of Cardiothoracic Surgery, Long Island Jewish Medical Center, New Hyde Park, New York

Success with peripheral arterial reconstruction using autogenous saphenous vein led to the use of allogenic saphenous vein in instances where saphenous vein was unavailable. With the advent of coronary artery bypass grafting, use of this conduit was applied to coronary reconstruction when conventional autogenous conduit was inadequate. However, follow-up angiography revealed graft patency rates of 15% at 6 to 12 months [1], 50% at 1 to 77 months [2], and 47% at 1 to 68 months [3], which were not improved by ABO matching.

See also page 826.

Clinical experience with allogenic vein for arterial reconstruction was preceded by experimental studies. Use of both fresh and frozen veins (protected with dimethyl sulfoxide) revealed equal patency in both groups, which declined to 69% in a limited follow-up of 5 to 7.5 months [4]. Tissue culture of the frozen vein suggested viability, which has been confirmed with recent sophisticated techniques [5]. Other experimental studies have focused on examining the mechanism for allogenic vein graft failure, whether it is related to rejection, and, if so, whether antigenicity can be altered by freezing or whether immunosuppressive therapy is effective in improving graft patency. Although the issue of rejection as a cause for allograft failure has been extensively debated, it is my bias that graft failure is clearly related to rejection with a sound piece of evidence provided by the observation that paired allografts (a donor dog provided two grafts for a single recipient) failed within 4 weeks of each other with a follow-up of 42 months [6]. It has been suggested that freezing of tissue alters its immunogenicity, and although a reduction in cellular infiltrate was noted after cryopreservation, there was no improvement in allograft patency [7]. Experimental demonstration of improved allograft patency with immunosuppressive therapy is lacking, but most studies have used low-dose therapy [7] because it did not seem wise to employ immunosuppression of the intensity required for solid organ transplantation and incur its attendant risks.

Clinical application of the latest technology for cryopreservation of allogenic vein for coronary reconstruction revealed a patency of 41% at a mean of 7 ± 2 months (range, 2 to 16 months), as reported in this issue of *The Annals* [8]. Thus, there is no evidence to suggest that arterialized allogenic vein graft patency has improved over the 15 years this graft has been employed in the coronary system or over the 37 years of use in the peripheral arteries. Low-dose immunosuppression has not been used clinically, but there is little evidence to support this approach. Although occasional patients will lack sufficient autogenous vein, the options have improved in recent years with the demonstration of 95% patency for the right gastroepiploic artery to 5 years. Inferior epigastric artery patency beyond 1 year remains to be established, but at that mark it is better than that for allogenic vein. Additionally, recent experience revives the radial artery as a viable conduit. Despite its reduced patency, arm vein has better patency than that reported for allogenic vein.

The limited patency of allogenic vein and the increasing attractiveness of alternative arterial conduits relegate use of the former to those rare situations where all leg and arm autogenous vein is unavailable, the internal thoracic arteries have been used, and it is not practical or feasible to use the alternative arterial conduits. The latter circumstance might be that of cardiogenic shock or an elective operation with severe impairment of ventricular function or a combined valve and coronary operation.

References

1. Gelbfish J, Jacobowitz IJ, Rose DM, et al. Cryopreserved homologous saphenous vein: early and late patency in coronary artery bypass surgical procedures. Ann Thorac Surg 1986;42:70–3.
2. Ochsner JL, Lawson JD, Eskind SJ, Mills NL, DeCamp PT. Homologous veins as an arterial substitute: long-term results. J Vasc Surg 1984;1:306–13.
3. Bical O, Bachet J, Laurian C, et al. Aortocoronary bypass with homologous saphenous vein: long-term results. Ann Thorac Surg 1980;30:550–6.
4. Barner HB, DeWeese JA, Schenk EQ. Fresh and frozen homologous venous grafts for arterial repair. Angiology 1966;17:389–401.
5. Brockbank KGM, Donovan TJ, Ruby ST, Carpenter JF, Hogen PO, Woodley MA. Functional analysis of cryopreserved veins. J Vasc Surg 1990;11:94–102.
6. Kraeger RR, Lagos JA, Barner HB. Long term evaluation of allogenic veins as arterial grafts. J Vasc Surg 1976;10:212–7.
7. Deaton DW, Stephens JK, Karp RB, et al. Evaluation of cryopreserved allograft venous conduits in dogs. J Thorac Cardiovasc Surg 1992;103:153–62.
8. Laub GW, Muralidharan S, Clancy R, et al. Cryopreserved allograft veins as alternative coronary artery bypass conduits: early phase results. Ann Thorac Surg 1992;54:826–31.

Address reprint requests to Dr Barner, Division of Cardiothoracic Surgery, Long Island Jewish Medical Center, New Hyde Park, NY 11042.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:817 • 0003-4975/92/$5.00

The Thoracic Surgery Directors Association (TSDA) Resident Research Award, sponsored by Medtronic, Inc, was established in 1990 to encourage resident research in cardiothoracic surgery. Abstracts submitted to The Society of Thoracic Surgeons (STS) Program Committee representing research performed by residents were forwarded to the TSDA to be considered for this award. The abstracts were reviewed by the TSDA Executive Committee consisting of: Martin F. McKneally, President; Gordon F. Murray, President-Elect; Mark B. Orringer, Secretary/Treasurer; Stanton P. Nolan, Executive Committeeman; and Sidney Levitsky, Executive Committeeman.

The second TSDA Resident Research Award was given to Dr Robert E. Maughan, resident in training at Maimonides Medical Center, Brooklyn, New York, who received a sum of $2,500 and had his expenses paid to the STS meeting.

The TSDA, with support by Medtronic, Inc, will make this award annually, using the above selection procedure. The resident author of the selected study will be recognized at the STS meeting.

Intrathecal Perfusion of an Oxygenated Perfluorocarbon Prevents Paraplegia After Aortic Occlusion

Robert E. Maughan, MD, Chittur Mohan, MD, Ira M. Nathan, PhD, Enrico Ascer, MD, Peter Damiani, BS, Israel J. Jacobowitz, MD, Joseph N. Cunningham, Jr, MD, and Corrado P. Marini, MD

Division of Thoracic and Cardiovascular Surgery, Department of Surgery, Maimonides Medical Center, Brooklyn, New York, and Polyclinic Medical Center, Harrisburg, Pennsylvania

A canine model was used to evaluate the effects of continuous intrathecal perfusion of an oxygenated perfluorocarbon emulsion on systemic and cerebral hemodynamics and neurologic outcome after 70 minutes of normothermic aortic occlusion. Twelve mongrel dogs were instrumented to monitor proximal and distal arterial blood pressure, cerebrospinal fluid pressure, spinal cord perfusion pressure, and somatosensory evoked potentials. The intrathecal perfusion apparatus consisted of two perfusing catheters, placed in the intrathecal space through a laminectomy, and a draining catheter percutaneously inserted in the cisterna cerebellomedullaris. The aorta was cross-clamped just distal to the left subclavian artery for 70 minutes. Animals were randomized into two groups: group 1 (n = 6) animals were treated with intrathecal perfusion of saline solution, whereas group 2 (n = 6) animals received oxygenated Fluosol-DA 20%. Data were acquired at baseline, during the cross-clamp period, and after reperfusion. Normothermic Fluosol or saline solution was infused at a rate of 15 mL/min beginning 15 minutes before cross-clamping and continued throughout the ischemic interval. There was no difference in proximal arterial blood pressure (97.2 versus 95.4 mm Hg; $p > 0.05$) or distal arterial blood pressure (14.6 versus 15.0; $p > 0.05$) between the two groups throughout the cross-clamp interval. Cerebrospinal fluid pressure rose significantly in both groups with the onset of intrathecal perfusion of either saline solution or Fluosol (7 ± 1 versus 24 ± 5 and 8 ± 1 versus 40 ± 4 mm Hg, respectively; $p < 0.05$). The rise in cerebrospinal fluid pressure was sustained throughout the perfusion interval in both groups. Negative spinal cord perfusion pressure values were recorded in both groups throughout the cross-clamp interval. All Fluosol-treated animals regained electrophysiologic conduction within 10 minutes of reperfusion and were spared neurologic injury. In contrast, all but 1 animal treated with saline solution suffered spastic paraplegia. Based on the results of this study, we conclude that the intrathecal space can be used as an alternate vascular tree to perfuse the spinal cord with an oxygenated perfluorocarbon emulsion. In this canine model, paraplegia after 70 minutes of normothermic aortic occlusion can be uniformly prevented by the intrathecal perfusion of normothermic Fluosol-DA 20%.

(Ann Thorac Surg 1992;54:818–25)

Despite recent improvements in anesthetic management, operative technique, and spinal cord protection, paraplegia continues to be a devastating complication of procedures requiring cross-clamping of the descending thoracic aorta. Although the etiology of paraplegia is multifactorial, the final common pathway to

---

Presented, in part, at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Marini, Polyclinic Medical Center, Harrisburg, PA 17110.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

spinal cord injury is ischemia of the spinal cord from either inadequate collateral blood flow during aortic cross-clamping or failure to reimplant critical intercostal vessels [1, 2]. The incidence of paraplegia is related to the depth and duration of ischemia; the risk of paraplegia increases from 0.5% for ischemic intervals shorter than 30 minutes to 95% to 100% after 60 minutes of ischemia [3, 4]. The incidence of paraplegia after repair of extensive dissecting thoracoabdominal aneurysms can be as high as 40% [5].

Efforts to reduce the incidence of paraplegia have centered on maintenance of distal aortic perfusion with shunts and bypasses [6, 7], rapid identification and reimplantation of critical intercostal vessels [8, 9], increasing spinal cord perfusion pressure with cerebrospinal fluid (CSF) drainage [10, 11], and mitigation of the effects of ischemia with pharmacological agents such as steroids [12], superoxide dismutase [13], and calcium-channel blockers [14]. Although such efforts have been shown to be of benefit both experimentally and clinically, there is currently no method available to uniformly prevent paraplegia after prolonged aortic occlusion.

Because the current modalities have been less than satisfactory in preventing paraplegia after prolonged cross-clamping, we decided to investigate an alternate means of perfusing the spinal cord during aortic occlusion. As the perfusion of the subarachnoid space with oxygenated perfluorocarbon emulsion has been shown to maintain electrical activity during brain ischemia [15], we investigated whether the intrathecal perfusion of Fluosol-DA 20% could prevent paraplegia after 70 minutes of normothermic aortic occlusion.

Material and Methods

Experimental Preparation

Twelve mongrel dogs weighing 25 to 35 kg were anesthetized with intravenous pentobarbital sodium (20 mg/kg). Animals were intubated and placed on a Harvard ventilator (Harvard Apparatus, Millis, MA) using room air. Respiratory settings included a tidal volume of 12 mL/kg, respiratory rate to maintain the partial pressure of carbon dioxide between 25 and 35 mm Hg, and 5 cm H_2O of positive end-expiratory pressure. Pressure monitoring catheters were inserted into the left carotid and femoral arteries and the left external jugular vein to monitor aortic pressures proximal and distal to the cross-clamp and central venous pressure, respectively. All pressures were monitored with Bentley Trantec physiological pressure transducers (Model 60-800; Santa Ana, CA). Lactated Ringer's solution was infused intravenously at a rate of 5 mL/kg/h. Through a left thoracotomy in the fourth intercostal space, the aorta was isolated 1 cm distal to the left subclavian artery. After aortic cross-clamping, partial exsanguination (removal of 40% of circulating blood volume) was used to maintain mean proximal arterial blood pressure between 85 and 95 mm Hg in both groups.

With the animal in a prone position, a lumbar laminectomy was performed. The spinous processes of L4 and L5 were removed, and the bone was shaved until the epidural fat was exposed. The dura over the cauda equina was exposed, and two cruciate incisions were made. Two polyethylene inflow catheters (PE90; Clay Adams, Division of Becton Dickinson & Co, Parsippany, NJ) were inserted into the intrathecal space and advanced for 2 cm along the lateral aspect of the cord, one directed cephalad and the other caudad. Purse string sutures of 6-0 Prolene (Ethicon, Somerville, NJ) were placed to close the dura around the catheters and prevent leakage of CSF. Using this technique, there was loss of less than 10 mL of CSF during the insertion of the catheters and no appreciable loss of Fluosol or saline solution during perfusion. The catheters were secured to the paraspinal muscles, exteriorized through the wound and connected to a Y connector. With the animal again in a right lateral decubitus position, a 20-gauge, 3.8-cm spinal catheter was percutaneously inserted into the cisterna cerebellomedularis to monitor CSF pressure (CSFP) and serve as a drainage catheter. The CSFP transducer was zero referenced to the level of the cisterna cerebellomedularis.

Somatosensory evoked potentials (SEPs) were monitored with a Nicolet IV apparatus (Nicolet, Madison, WI) after cortical electrodes and a right posterior tibial nerve stimulator were placed.

Preparation and Delivery of Fluorocarbon Emulsion

Fluosol DA-20% emulsion (The Green Cross Corporation, Osaka, Japan) consists of three separate parts that must be mixed before use: (1) the Fluosol emulsion; (2) solution 1; and (3) solution 2. The additive solutions serve to adjust pH ionic strength and osmotic pressure in the final 20% emulsion, and must be added separately and sequentially before administration. Solution 1 contains sodium bicarbonate and potassium chloride; solution 2 contains sodium chloride, dextrose, magnesium, and calcium. Before use, the emulsion was thawed and preoxygenated to an oxygen content greater than 5.5 vol% by bubbling a 95% O_2 and 5% CO_2 mixture at 2 L/min for 20 minutes; thereafter, this level of oxygenation was maintained with continuous bubbling of the same gas mixture at 2 L/min throughout the cross-clamp interval. Temperature of the emulsion was maintained between 32° and 37°C by placement in a water bath.

The delivery system consisted of Fluosol emulsion suspended 1 m above the animal. Perfusion occurred by gravity at a flow rate of 12 to 15 mL/min through polyethylene tubing connected to the two inflow catheters positioned in the cauda equina. Drainage was assured by the spinal catheter placed in the cisterna cerebellomedularis, and the antigravitary return of the solution to the suspended reservoir was provided by a roller pump. Cerebrospinal fluid pressure was maintained at less than 50 mm Hg throughout the experiment. Oxygen content of the emulsion was measured at the inflow and outflow sites using Lex-O_2-Con apparatus (Lexington Instruments Corp, Waltham, MA); oxygen extraction ratio was calculated by dividing the difference between inflow and outflow content by inflow content.

To evaluate whether normal saline solution could be used to oxygenate the spinal cord, we oxygenated normal saline solution in the same fashion and measured the oxygen content of samples obtained from the inflow and outflow catheters. The oxygen content was 0.3 vol% at both sites, indicating inadequate oxygen content and absence of extraction; therefore, we decided to omit oxygenation of the solution in the group receiving normal saline solution.

After the acquisition of baseline hemodynamics, animals were randomly assigned to two groups: group 1 animals (n = 6) underwent intrathecal perfusion with normothermic saline solution beginning 15 minutes before aortic cross-clamping and throughout the 70-minute cross-clamp interval. Group 2 animals (n = 6) underwent normothermic intrathecal perfusion with oxygenated Fluosol at the same flow rates throughout the same ischemic interval. Hemodynamic parameters and SEPs were monitored at 5-minute intervals during the 70-minute cross-clamp period and for 30 minutes after reperfusion.

After removal of the aortic cross-clamp, the thoracotomy was closed over a thoracostomy tube, which was removed upon reversal of anesthesia. The inflow catheters were removed and the dura closed with 6-0 Prolene sutures. A matrix of bone chips and bone wax was placed into the bony defect for added stability, and the lumbar laminectomy was closed. A Penrose drain was placed in the subcutaneous tissue and exteriorized through a separate stab incision to prevent seroma formation. All animals received, preoperatively, 1 g of cefazolin intravenously.

Postoperative Evaluation

Animals were evaluated at 24 and 48 hours postoperatively, and neurologic function was graded according to Tarlov's score by an observer unaware of the experimental protocol. At 48 hours all animals were anesthetized with intravenous pentobarbital sodium (20 mg/kg), laminectomy was performed, and the spinal cord was removed and fixed in 10% formalin. Animals were then killed by intravenous injection of a lethal dose of potassium chloride.

All animals received care in compliance with the "Principles of Laboratory Animal Care" (formulated by the National Society for Medical Research) and the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985).

Statistical Method

All data are presented as means ± standard error of the mean, and were analyzed with analysis of variance for repeated measures. When present, differences were localized by the method of Newman and Keuls. Somatosensory evoked potential data and neurologic outcome were analyzed with Fisher's exact test. Statistical significance was accepted to correspond to a p value of less than 0.05.

Results

Hemodynamics

The intrathecal perfusion of saline solution, before aortic cross-clamping, caused an immediate rise in baseline systemic blood pressure: blood pressure rose from 88 ± 4 mm Hg to 119 ± 6 mm Hg ($p < 0.05$). In contrast, the intrathecal perfusion of Fluosol, before aortic occlusion, did not cause any significant change in systemic blood pressure (85 ± 4 mm Hg at baseline versus 83 ± 4 mm Hg during Fluosol infusion; $p > 0.05$) (Fig 1). There was no significant difference in distal arterial blood pressure between the two groups after aortic cross-clamping (15 ± 3 versus 15 ± 3 mm Hg; $p > 0.05$) (Fig 2).

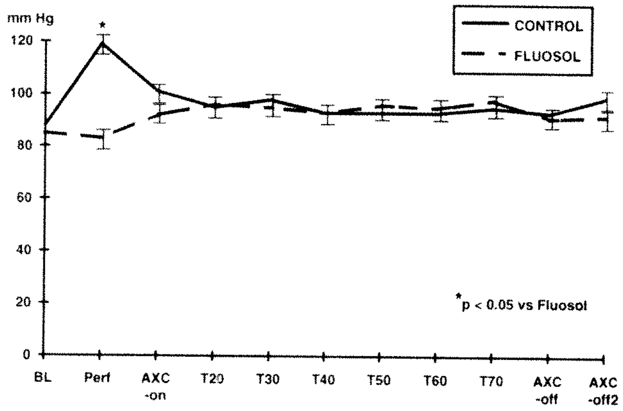


Fig 1. Time course of proximal blood pressure in control (saline) and Fluosol-treated animals. (AXC-off = *removal of aortic cross-clamp;* AXC-off2 = *thirty minutes after reperfusion;* AXC-on = *application of aortic cross-clamp;* BL = *baseline;* Perf = *intrathecal perfusion of saline or Fluosol;* T20–T70 = *20, 30, 40, 50, 60, and 70 minutes after aortic cross-clamping.)*

Spinal Fluid Dynamics

Cerebrospinal fluid pressure increased significantly from a baseline value of 7 ± 1 to 24 ± 5 mm Hg ($p < 0.05$) with the onset of intrathecal perfusion with saline solution. Intrathecal perfusion with Fluosol caused an even greater rise in CSFP (8 ± 1 at baseline versus 40 ± 4 mm Hg; $p < 0.05$). The CSFP during the infusion of Fluosol was significantly higher than that observed during saline infusion (40 ± 4 versus 24 ± 5 mm Hg; $p < 0.05$). The rise in CSFP persisted throughout the cross-clamp interval in both groups (Fig 3). The sustained rise in CSFP, in the presence of low distal arterial blood pressure after aortic cross-clamping caused negative spinal cord perfusion

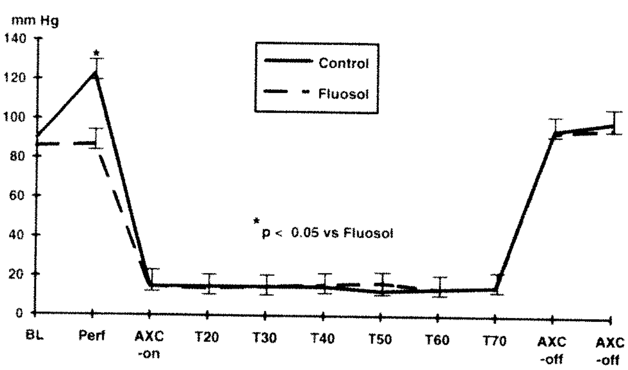


Fig 2. Time course of distal blood pressure for control (saline) and Fluosol-treated groups. (Abbreviations are as in Figure 1.)

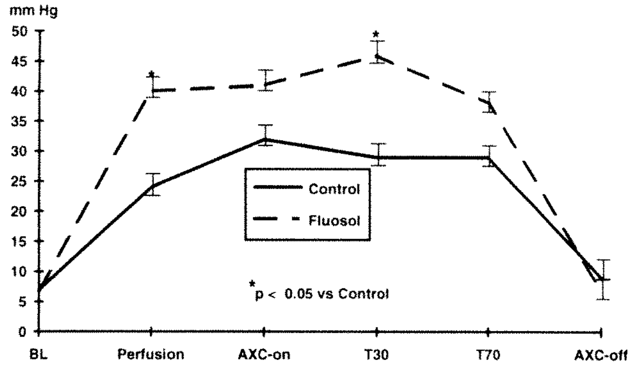


Fig 3. Time course of cerebrospinal fluid pressure for control (saline) and Fluosol-treated groups. (Abbreviations are as in Figure 1.)

pressure throughout the cross-clamp interval in both groups (group 1, −14.5 ± 7 mm Hg; group 2, −22.9 ± 5 mm Hg) (Fig 4).

After reperfusion, systemic hemodynamics and cerebrospinal fluid pressures returned to baseline values.

Somatosensory Evoked Potential Return and Neurologic Outcome

All Fluosol-treated animals regained electrophysiologic conduction within 10 minutes of reperfusion, whereas only one of the saline-treated animals displayed a similar response ($p < 0.01$). The return of SEPs correlated with neurologic outcome. All but 1 animal in group 1 (saline perfusion) suffered spastic paraplegia upon recovery from anesthesia; at reevaluation at 24 and 48 hours postoperatively, they had not improved neurologically. In contrast, all of the Fluosol-treated animals were spared neurologic injury ($p < 0.01$).

Oxygen Extraction

Mean oxygen content of Fluosol at the inflow catheter was significantly higher than that measured at the outflow catheter (5.293 ± 0.144 versus 3.686 ± 0.096 vol%; $p < 0.01$). The oxygen extraction ratio was 29.6% (Fig 5).

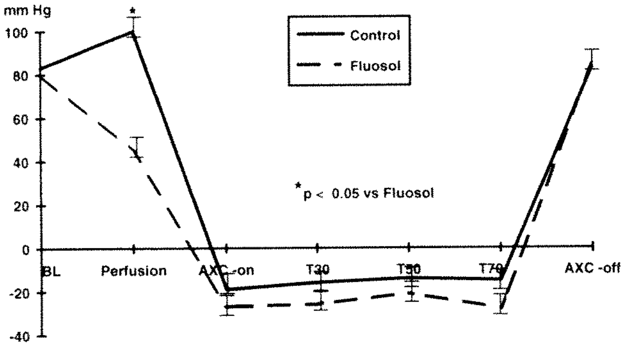


Fig 4. Time course of spinal cord perfusion pressure for control (saline) and Fluosol-treated groups. (Abbreviations are as in Figure 1.)

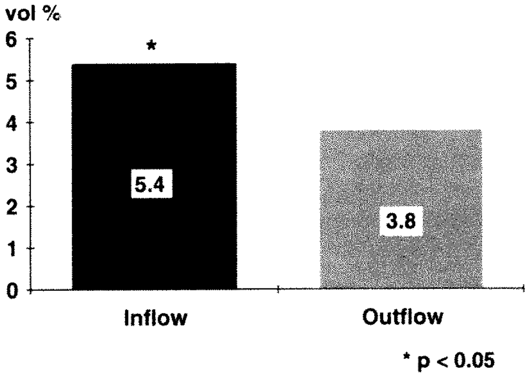


Fig 5. Comparison of oxygen content of Fluosol samples from the inflow and outflow catheters.

Histologic Examination

No significant difference in pathology of cord tissue was detected using light microscopy. There was no evidence of arachnoid or meningeal inflammation in either group.

Comment

Inherent to repair of descending thoracic and thoracoabdominal aortic aneurysms is temporary occlusion of the descending thoracic aorta with the inevitable occurrence of transient spinal cord ischemia, if adjunctive measures are not implemented to provide distal aortic perfusion. However, paraplegia cannot be uniformly prevented, even when distal aortic perfusion is provided with mechanical devices [16]. Other modalities employed to reduce the unacceptably high risk of paraplegia after procedures on the thoracic and thoracoabdominal aorta include methods to detect intraoperatively spinal cord ischemia with SEPs or motor evoked potentials [17, 18], reimplantation of critical intercostal vessels identified with hydrogen-induced current impulse technique [19], and drainage of CSF to increase spinal cord perfusion [11, 20]. Although all of these techniques have shown some experimental or clinical success, they have not been uniformly successful in eliminating the risk of postoperative paraplegia.

The two major causes of postoperative paraplegia after procedures on the thoracic and thoracoabdominal aorta are (1) the degree of ischemia, which is related to the extent of the aneurysmal disease, the degree of collateralization, and the duration of the ischemic interval [21, 22], and (2) failure to reimplant, in the graft, intercostal vessels that supply the spinal cord [23]. Therefore, the approaches used to prevent paraplegia after aortic cross-clamping have been directed at balancing the two major risk factors for neurologic injury: provide distal aortic perfusion with mechanical devices and identify and reimplant critical intercostal vessels. The pitfalls of these approaches are the inability to uniformly protect the spinal cord with retroperfusion even when "adequate" distal aortic blood pressure is achieved and the prolongation of the ischemic interval required to anastomose critical intercostal vessels, as well as the necessity to declamp the proximal aorta to reestablish perfusion through the reattached arteries to provide blood supply to the spinal cord.

It is for this reason that we decided to investigate a new approach that involves the use of the intrathecal space to provide oxygen to the spinal cord. This approach, if successful, would allow the surgeon ample time to reimplant all intercostal vessels without time constraints and would not require proximal declamping after reattachment of the intercostal arteries.

Because previous studies have demonstrated the ability of oxygen to diffuse from the subarachnoid space across the ependyma and maintain electrical activity in brains subjected to ischemia [15], we decided to use the intrathecal space as an alternate vascular tree to perfuse the spinal cord during a period of prolonged normothermic aortic occlusion.

To provide a high diffusion gradient sufficient to allow passive diffusion of oxygen across the ependyma to the external white matter and the central gray matter, oxygenated Fluosol-DA 20%, a perfluorocarbon emulsion, was used. This agent was selected because of its ability to deliver substantial amounts of oxygen without apparent tissue toxicity [24]. The combined surface area of the Fluosol particles is larger than that of blood (1.82×10^8 cm^2/L versus 1.86×10^6 cm^2/L, respectively), the time taken for oxygen exchange or release is twice as fast as hemoglobin, and the time of CO_2 transfer is a few milliseconds [25]. In addition to having excellent oxygen transport properties, Fluosol may prevent vasospasm, reach areas of ischemia through collateral microcirculation, and inhibit the CD11 receptors of polymorphonuclear cells, therefore preventing leukocyte aggregation and diapedesis. Additionally, Fluosol has been successfully used in the laboratory setting to minimize reperfusion injury after normothermic ischemia of the myocardium and skeletal muscles [26, 27].

In the present study, the intrathecal perfusion of saline solution in control animals caused a significant rise in systemic blood pressure, whereas Fluosol perfusion did not affect systemic blood pressure. This differential response to intrathecal perfusion can be explained by the difference in pH between the two solutions used in this study: the pH of normal saline solution is 5.0, whereas the pH of Fluosol-DA 20% is 7.40. The infusion of normal saline solution in the intrathecal space caused systemic hypertension, probably through a direct stimulation of the vasomotor center. In contrast, Fluosol can be safely infused in the intrathecal space because it has the characteristics of CSF with regard to pH, electrolyte content, and osmotic pressure [24]. After aortic cross-clamping there was no significant difference in systemic pressures between the two groups because the pressures were controlled with partial exsanguination to prevent proximal hypertension.

Cerebrospinal fluid pressure rose significantly, in both groups, during the intrathecal perfusion. This response is not surprising because CSF was not drained before the onset of intrathecal perfusion; hence, there was an increase in CSF volume which can explain the rise in CSFP. Because in this study, we did not have a group in which CSF was drained before the onset of intrathecal perfusion to prevent the volume expansion of the CSF, we cannot say whether removal of CSF will prevent or minimize the increase in CSFP. The higher pressures seen with Fluosol perfusion may be attributed to the higher viscosity of Fluosol (2.7 centipoise at shear rate of $77\ s^{-1}$ at 37°C) as compared with saline solution. Fluosol is a non-Newtonian fluid like blood, and although it has lower viscosity than blood at lower shear rates, it does have higher viscosity than saline solution. Therefore, we believe that the intrathecal perfusion of Fluosol-DA 20% will cause a rise in CSFP, even if CSF volume is drained before the onset of perfusion.

The elevation in CSFP in the presence of decreased distal blood pressure after cross-clamping resulted in negative spinal cord perfusion pressure, defined as the difference between distal arterial blood pressure and CSFP, throughout the cross-clamp interval in both groups. Therefore, as previously shown in our laboratory [11], in the absence of adjunctive measures, all animals should have suffered spastic paraplegia.

Somatosensory evoked potentials were monitored at baseline, during the cross-clamp interval, for 30 minutes after reperfusion, and at 48 hours postoperatively. In all animals, SEPs were lost 5 to 12 minutes after placement of the aortic cross-clamp, and there was no difference between the two groups. We believe that the loss of SEPs during the intrathecal perfusion may be attributed to a small decrease in temperature of the spinal cord caused by the intrathecal perfusion. However, all of the Fluosol-treated animals regained electrophysiologic conduction within 10 minutes of reperfusion, whereas only 1 of the saline-treated animals displayed a similar response. The return of SEPs correlated with neurologic outcome. All of the Fluosol-treated animals were spared neurologic injury; in contrast, all but 1 of the saline-treated animals had spastic paraplegia at 48 hours. Obviously, because the temperature of the solutions varied from 32°C to 37°C, one could question whether the protective effect on the spinal cord was secondary to hypothermia or actual oxygenation. Although local hypothermia achieved with intrathecal perfusion of cold saline solution has been shown to be protective for relatively short ischemic intervals [28], we do not believe that the relatively small variations in perfusate temperature played a major role in our experiment. Hypothermia has been shown to reduce oxygen consumption of neural tissue by 5% for each degree of temperature drop between 37° and 22°C [29]; therefore, with a maximum drop of 5°C, the decrease in oxygen consumption would have been at most 25%, not adequate to provide sufficient protection for the ischemic interval chosen in this study. It is well known that spinal cord temperature must be lowered to 18° to 20°C to prevent ischemic injury to the spinal cord [30]. Furthermore, the statistically significant difference in oxygen content between the samples obtained from the inflow and outflow catheters with an extraction ratio of 29.6% indicates, indirectly, that protection to the spinal cord was afforded by the delivery of oxygen to the cord.

Of interest, the only animal in the control group that was spared paraplegia regained electrophysiologic conduction within 10 minutes of reperfusion. This animal displayed positive spinal cord perfusion pressure throughout the ischemic interval, with a mean greater than 10 mm Hg, a threshold value for spinal cord integrity in the canine model [11].

Based on the results of this study, we believe that it may be possible to use the intrathecal space as an alternate vascular tree to perfuse the spinal cord during periods of prolonged aortic occlusion. The intrathecal perfusion of an oxygenated perfluorocarbon emulsion can uniformly prevent paraplegia after extended normothermic aortic cross-clamping in the canine model. From the results of the oxygen extraction, it seems reasonable to conclude that the mechanism of spinal cord protection is by delivery of oxygen to the cord by passive diffusion across the ependyma. Additionally, the intrathecal perfusion of Fluosol may provide a "washout" of toxic metabolites and reduce reperfusion injury. Further investigations should address whether this perfusion can be accomplished through a double-lumen catheter inserted percutaneously in the intrathecal space, and whether the changes in CSF dynamics caused by this methodology can be minimized by changing flow rate and viscosity of the perfusate.

Supported by a grant from the Maimonides Research and Development Foundation. Additional support provided by Cardiothoracic Surgical Associates.

We gratefully acknowledge Anthony Siconolfi for technical operative assistance and Mary Ann Bottali for manuscript preparation.

References

1. Wadouh F, Lindeman E, Arndt CF, et al. The arteria radicularis magna anterior as a decisive factor influencing spinal cord damage during aortic occlusion. J Thorac Cardiovasc Surg 1984;88:1–10.
2. Williams GM, Perler BA, Burdick JF, et al. Angiographic localization of spinal cord blood supply and its relationship to postoperative paraplegia. J Vasc Surg 1991;13:23–35.
3. Katz NM, Blackstone EH, Kirklin JW, et al. Incremental risk factors for spinal cord injury following operations for acute traumatic transection. J Thorac Cardiovasc Surg 1981;81:669–74.
4. Jex RK, Schaff HV, Piehler JM, et al. Early and later results following repair of dissections of the descending thoracic aorta. J Vasc Surg 1991;3:226–37.
5. Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long term results of operations in 605 patients. J Vasc Surg 1986;3:389–404.
6. Grossi EA, Kreiger KH, Cunningham JN Jr, et al. Venoarterial bypass: a technique for spinal cord protection. J Thorac Cardiovasc Surg 1985;89:228–34.
7. Svensson LG, Von Ritter CM, Groeneveld HT, et al. Cross-clamping of the thoracic aorta. Influence of aortic shunts, laminectomy, papaverine, calcium channel blocker, allopurinol, and superoxide dismutase on spinal cord blood flow and paraplegia in baboons. Ann Surg 1986;204:38–47.
8. Laschinger JC, Cunningham JN Jr, Baumann FG, et al. Monitoring of SEP during surgical procedures on the thoracoabdominal aorta; III: Intraoperative identification of vessels critical to spinal cord blood supply. J Thorac Cardiovasc Surg 1987;94:271–4.
9. Svensson LG, Patel V, Robinson MF, et al. Influence of preservation or perfusion of intraoperatively identified spinal cord blood supply on motor evoked potentials and paraplegia after aortic surgery. J Vasc Surg 1991;13:355–65.
10. McCullough JL, Hollier LH, Nugent M. Paraplegia after thoracic aortic occlusion: influence of cerebrospinal fluid drainage. J Vasc Surg 1988;9:153–60.
11. Grubbs P, Marini CP, Toporoff B, et al. Somatosensory evoked potentials and spinal cord perfusion pressure are significant predictors of postoperative neurologic dysfunction. Surgery 1988;104:216–23.
12. Laschinger JC, Cunningham JN Jr, Cooper MM, et al. Prevention of ischemic spinal cord injury following aortic cross-clamping: use of corticosteroids. Ann Thorac Surg 1984;38:500–7.
13. Lim KH, Connolly M, Rose D, et al. Prevention of reperfusion injury of the ischemic spinal cord: use of recombinant superoxide dismutase. Ann Thorac Surg 1986;42:282–6.
14. Gelbfish JS, Phillips T, Rose DM, et al. Acute spinal cord ischemia: prevention of paraplegia with verapamil. Circulation 1986;74(Suppl 1):5–10.
15. Osterholm JL, Alderman JB, Triolo AJ, et al. Severe cerebral ischemia treatment by ventriculosubarachnoid perfusion with an oxygenated fluorocarbon emulsion. Neurosurgery 1983;13:381–7.
16. Crawford ES, Mizhari EM, Hess KR, et al. The impact of distal aortic perfusion and somatosensory evoked potential monitoring on prevention of paraplegia after aortic aneurysm operation. J Thorac Cardiovasc Surg 1988;95:357–67.
17. Cunningham JN Jr, Laschinger JC, Spencer FC, et al. Monitoring of SEP during surgical procedures on the thoracoabdominal aorta: IV. Clinical observations and results. J Thorac Cardiovasc Surg 1987;94:275–85.
18. Laschinger JC, Owen J, Rosenbloom M, et al. Direct noninvasive monitoring of spinal cord motor function during thoracic occlusion: use of motor evoked potentials. J Vasc Surg 1988;7:161–71.
19. Svensson LG, Patel V, Robinson MF, et al. Influence of preservation or perfusion of intraoperatively identified spinal cord blood supply on spinal motor evoked potentials and paraplegia after aortic surgery. J Vasc Surg 1991;13:355–65.
20. Bower GT, Murray MJ, Gloviczki P, et al. Effects of thoracic aortic occlusion and cerebrospinal fluid drainage on regional spinal cord blood flow in dogs: correlation with neurologic outcome. J Vasc Surg 1988;9:135–44.
21. Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. J Vasc Surg 1986;3:389–404.
22. Crawford ES, Palamara AE, Saleh SA, Roehm JOF. Aortic aneurysms: status of surgical treatment. Surg Clin North Am 1979;59:597–636.
23. Laschinger JC, Izumoto H, Kouchoukos NT. Evolving concepts in prevention of spinal cord injury during operations on the descending thoracic and thoracoabdominal aorta. Ann Thorac Surg 1987;44:667–74.
24. Hansebout RR, van der Jagt RCH, Sohal SS, Little JR. Oxygenated fluorocarbon perfusion as treatment of acute spinal cord compression injury in dogs. J Neurosurg 1981;55:725–32.
25. Naito R, Yokoyama K. Perfluorochemical blood substitutes Fluosol 43, Fluosol-DA-20% and 35%. In: Technical information booklet, Serial No. 5. Osaka, Japan: Green Cross Corporation, 1978.
26. Kolodgie FD, Virmani R, Farb A. Limitation of no reflow injury by blood-free reperfusion with oxygenated perfluorochemical (Fluosol-DA 20%). J Am Coll Cardiol 1991;18:215–23.
27. Forman MB, Bingham SE, Kopelman HA, et al. Reduction of

infarct size with intracoronary perfluorochemical in a canine preparation of reperfusion. Circulation 1985;71:1060–8.

28. Beurger R, Porto J, Fedoronko BS, et al. Selective deep hypothermia of the spinal cord prevents paraplegia after aortic cross-clamping in the dog model. J Vasc Surg 1992;15:62–72.

29. Hagerdal M, Harp J, Nilsson L, et al. The effect of induced hypothermia upon oxygen consumption in the rat brain. J Neurochem 1975;24:311–6.

30. Hansebout RR, Kuchner EF, Romero-Sierra C. Effects of local hypothermia and of steroids upon recovery from experimental spinal cord compression injury. Surg Neurol 1975;4:531–5.

DISCUSSION

DR AHMAD RAJII-KHORASANI (Neptune, NJ): I would like to thank The Society for this opportunity and congratulate the authors for their award. I see some wrinkles in the literature on thoracic aortic surgery, and in the interest of time I am going to discuss only the issue of transspinal perfusion pressure. There are two parameters in this measurement. One of them is distal aortic pressure, the other one is spinal fluid pressure. Let's look at them carefully.

The confined cranial-spinal space contains brain, meninges, vessels, and CSF. Because it is confined, any change in the volume of this space will cause a change in CSF pressure. Cerebrospinal fluid volume and its dynamics and the volume of brain and meninges are probably not affected by aortic clamping; however, the vascular volume is likely to be affected by clamping of the aorta. We know from own clinical experience that increasing the jugular venous pressure will increase the CSF pressure, cough or increased intrathoracic pressure increases CSF pressure, hypertension increases CSF pressure, and animal experiments have shown that if you increase cardiac output with hypervolemia you will have an increase in CSF pressure. The interesting thing that the same studies have shown is that not only is the CSF pressure increased, but also there is an increase in cortical blood flow. So what we do not know is what CSF pressure means. Is it a protective mechanism for some reason, for brain against, let's say, increased intravascular pressure, or is it a harmful effect? If it is a harmful effect, what are the ranges, when does it become harmful? The neurosurgical model of severe increased intracranial pressure where we see impedance of blood flow to the brain is perhaps the end of the spectrum and should not be adopted in any other circumstance. So let's look for a moment at the arterial pressure.

In the clinical model, as soon as you cross-clamp the aorta, when you use a pump or a partial bypass or a shunt you have three different areas of pressure, potential pressure for spinal cord in your system, and in this experiment you have two areas. The proximal pressure, which is usually elevated, could be your spinal perfusion pressure. In fact all the cases that the surgeons do with the so-called clamp and go, during their clamp the only circulation to their spinal cord is going through the cephalic source of circulation. So that is the spinal perfusion pressure.

On the other hand, if you use a partial bypass or a shunt and you are hoping to take advantage of possible distal position of the spinal cord circulation or the retrograde collaterals, then you add to that the potential of that pressure to be your spinal cord perfusion pressure, or it might be your only spinal cord perfusion. It depends on the anatomy. And in the patients whom you have operated on who have had adequate proximal circulation and adequate distal circulation but became paraplegic, then your excluded segment pressure was your spinal cord perfusion pressure.

Now, in relation to the arterial pressure elevation with clamping and the elevated CSF pressure, if the mechanism is vascular engorgement, if suddenly we are exposing the proximal circulation to the same or slightly reduced cardiac output, we will see the cerebral circulation as increased cardiac output, which was demonstrated to increase your cerebral blood flow. So if the engorgement is the cause of increased pressure, then it is no surprise that when you give patients nitrite you will have your CSF pressure go up, but did you measure the blood flow to show that there is a decrease in blood flow? I do not know if it is really accurate to do this mathematical measurement using only your distal pressure.

So the question I have is, what does it mean in physical terms, in mechanical terms, when you have a negative transspinal perfusion pressure? My second question is, in your second group was there a significant drop in your proximal blood pressure?

DR MAUGHAN: Thank you, Dr Khorasani. Let me answer your last question concerning negative spinal cord perfusion pressures measured as the difference between distal blood pressure and CSF pressure. Negative spinal cord perfusion pressures are uniformly associated with absence of meaningful spinal cord blood flow as measured with radioisotopes and are associated with a paraplegia rate of 100% in animal models. In this experiment, the intrathecal infusion of both saline and Fluosol solutions caused an increase in CSF pressure; this in turn resulted in negative spinal cord perfusion pressures. Therefore, based on previous studies in our laboratory, all animals should have suffered spastic paraplegia. What is remarkable is that although Fluosol-treated animals had lower spinal cord perfusion pressures compared with saline-treated animals, none of them suffered neurologic injury.

DR LARS G. SVENSSON (Houston, TX): I would also like to congratulate the authors on a very fine study and potentially a major breakthrough in the prevention of paraplegia. Since our early work in 1985 we have believed that the use of the intrathecal space was the way to protect the spinal cord, and in 10 animals no paralysis resulted with intrathecal papaverine. We use intrathecal papaverine in patients, and it reduces the incidence of immediate postoperative paraplegia and paralysis. The problem we have encountered in patients, however, particularly in association with hypotension or respiratory failure, is delayed development of paraplegia. Similarly, I think your technique will be effective in probably two-thirds of the patients in preventing immediate postoperative paraplegia, particularly in the patients with short proximal descending thoracic aortic aneurysms, in whom ischemia to the cord is probably the predominant cause of the paraplegia. In the more extensive thoracoabdominal aortic aneurysm, intercostal artery reimplantation becomes probably more important. I have a few questions.

First of all, in the neurology literature it has been said that when one studies brain oxygenation, oxygen will only diffuse from the surface of the brain to about a depth of 1 mm into the cortex. My question is, have you thought about looking at the oxygenation of the spinal cord both on its surface and deeper inside the spinal cord? This could easily be done with a polygraphic technique of measuring oxygen with a fine needle. Excellent probes are available for this.

Second, I might have misunderstood you, but did you measure the temperature of your Fluosol before you perfused the spinal cord? Was it possibly cold? In other words, are you mimicking the study of Ramon Berguer in which he showed that intrathecal cooling of the spinal cord was equally protective? Was the Fluosol inflow and effluent oxygenation significantly different? Because Fluosol has some vasodilatory effects like papaverine but normal saline solution will probably cause spasm, might some of the effect of your high paraplegia rate in the control group been due to spasm in that group, and vasodilatation been the protective effect in the Fluosol group? Nevertheless, 70 minutes of aortic cross-clamping in a dog model will virtually always result in paraplegia. Finally, do you have any thoughts about the use of something like this in humans? Have you thought about the problem of getting FDA approval or any other way of trying to apply the technique to humans?

If this technique proves to be effective in humans, it could be a major breakthrough. Reimplantation of the intercostal vessels, however, continues to be a problem.

DR MAUGHAN: Thank you, Dr Svensson. From the neurological literature there are examples of local perfusion of the spinal cord with oxygenated perfluorocarbons, and what they found was that you required a 600 mm Hg gradient to have passive diffusion of the oxygen across the ependyma and into the spinal cord. Although we did not measure specifically whether or not there was oxygenation of the cord, we used the measurement of oxygen content, via the inflow and outflow catheters, as an indirect method of oxygen consumption. Future work, which we have already begun, is to examine more closely the exact mechanism by which Fluosol works and the exact mechanism of oxygen uptake.

As far as measuring the temperature of the Fluosol, this is a very pertinent question because we are oxygenating the Fluosol during the experiment, and the question arises whether or not the protective effects may be the result of some degree of hypothermia. We measured temperature at the inflow catheter and found that it ranged from an initial temperature of 37°C down to a low of 32°C at 60 minutes of the experiment. Based on previous studies, which show a decrease in metabolic rate of 5% per degree of temperature drop, this would result in a maximum 25% decrease in metabolic rate toward the end of the experiment. This would not be enough to explain the protective effects of the Fluosol.

The third question concerned the effects of saline solution being due to vasospasm. That is a very pertinent question. In fact we noticed that the saline infusion did elicit some type of vasomotor response with a resultant hypertension. This could have also resulted in some vasospasm in the spinal canal. But, as you suggested, the 70-minute cross-clamp interval would have resulted in paraplegia whether we had infused saline solution or not, based on previous experiments.

As far as clinical application, we are currently working on a more clinical approach to this problem by development of an infusion and drainage apparatus that can be inserted percutaneously into the lumbar area. This may make this approach more clinically applicable. As far as FDA approval of Fluosol, I think we will just have to wait and see how far the animal experimentation can go and if we can document the lack of adverse effects of the Fluosol.

Cryopreserved Allograft Veins as Alternative Coronary Artery Bypass Conduits: Early Phase Results

Glenn W. Laub, MD, S. Muralidharan, MD, Robert Clancy, RN, W. Jay Eldredge, MD, Chao Chen, PhD, Mark S. Adkins, MD, Javier Fernandez, MD, William A. Anderson, MD, and Lynn B. McGrath, MD

Division of Cardiothoracic Surgery, Deborah Heart and Lung Center, Browns Mills, New Jersey, and Department of Surgery, University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School, New Brunswick, New Jersey

Traditional autologous conduits are sometimes unavailable or unsuitable to permit total revascularization during coronary artery bypass grafting. In these patients the results of using nonautologous alternative conduits has been disappointing. Encouraged by the excellent long-term results seen with cryopreserved allograft valves, a clinical protocol was developed to evaluate the use of a commercially cryopreserved allograft saphenous vein (CPV). Our protocol consisted of using CPV when left internal mammary arteries and autologous saphenous vein grafts were unavailable or unsuitable for complete revascularization. Blood group (ABO) typed CPVs were thawed and implanted as required using standard surgical techniques. From December 1989 through June 1991, 19 of 1,602 patients who underwent coronary revascularization had CPVs implanted (1.2%). There were no operative deaths. An attempt was made to evaluate the patency of all grafts with coronary arteriography or ultrafast computed tomographic scans. Fourteen patients were available for patency evaluation. Patency rate in the 14 patients studied at a mean of 7 ± 2 months (range, 2 to 16 months) were: internal mammary artery, 93% (14/15); saphenous vein graft, 80% (4/5); and CPV, 41% (7/17). The patency of the CPV was significantly less than the patency rate for the saphenous vein and internal mammary artery ($p = 0.004$). We conclude that the short-term patency rate of CPVs is inferior to that of autologous vessels. Due to its poor patency, we recommend that CPV should only be used when no other autologous conduit is available.

(Ann Thorac Surg 1992;54:826–31)

Autologous internal mammary arteries (IMAs) and saphenous vein grafts have traditionally been the conduits of choice for coronary revascularization [1–3]. However, in certain situations they are unavailable, unusable, or unsuitable. Cryopreserved allograft saphenous vein (CPV) conduits harvested from young cadavers have recently become commercially available. Although previous studies of allograft saphenous vein grafts reported poor patency [4–6], advances in cryopreservation techniques have experimentally shown promising results [7–10]. Cryopreservation has been shown to preserve cellular viability and structural integrity and to possibly decrease immunologic response to transplantation [7, 9, 10], and initial clinical trials with CPV are encouraging with actuarial allograft patency of more than 85% at 12 months (K.G.M. Brockbank, PhD, CryoLife Cardiovascular Inc; personal communication). However, only a small percentage of patients who had this new CPV implanted underwent patency follow-up.

For editorial comment, see page 817.

As a result of positive early clinical and experimental results, we implemented a clinical protocol to evaluate CPV patency in patients undergoing coronary revascularization who had unavailable, inadequate, or unsuitable autologous IMAs and saphenous veins for complete revascularization.

Material and Methods

A protocol for the management of patients with inadequate autologous saphenous veins for complete coronary revascularization was developed and approved by our institutional review board. All patients scheduled for coronary revascularization underwent routine examination to determine the availability and suitability of lower extremity veins. Patients with a history or evidence of bilateral saphenous vein harvesting, advanced venous insufficiency, or severe varicose veins who required vein grafts were considered as potential candidates for receiving CPV. In these cases informed consent for the possible use of the CPV was obtained preoperatively. If the need for CPV became apparent during the operation, informed consent was obtained from the patient's legal representative.

Presented at the Twenty-Eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Laub, Deborah Heart and Lung Center, Browns Mills, NJ 08015.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Patient Population

From December 1, 1989, through June 30, 1991, 1,602 patients underwent coronary revascularization. Nineteen of these patients required cryopreserved vein implantation (1.2%). Cryopreserved allograft saphenous veins were used in 8 patients because the native lower extremity veins had been previously harvested. In an additional 11 patients, the native veins were of unsatisfactory quality due to thrombophlebitis, varicosities, inappropriate vessel caliber, or excessive wall thickness. Five of the patients who received CPVs were identified preoperatively as likely to require alternative conduits, and 14 patients were found to have unusable saphenous veins intraoperatively and had an unscheduled use of CPVs. Ten patients were male, and the mean age of all patients was 65 ± 7.3 years (range, 53 to 76 years). Sixteen of the patients were in functional class III or IV. Fifteen patients underwent isolated coronary revascularization and 4 patients underwent a concomitant valve operation with coronary revascularization. Thirteen of the operations were primary and 6 were reoperative procedures. At least one IMA was used in 17 patients and both IMAs were used in 2 patients. In the 2 patients who did not receive an IMA graft, the IMA had already been harvested at a previous cardiac procedure. Bilateral IMAs were used very selectively during this study. At the time it was our policy not to use both IMAs in patients with diabetes, advanced age, or hemodynamic instability.

Operative Technique

The operative technique consisted of total cardiopulmonary bypass using moderate systemic hypothermia and a membrane oxygenator. Bypass was initiated at flow rates of $2.2\ \text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ and decreased to $1.6\ \text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ for core temperatures less than 30°C. Cold cardioplegia was used to achieve diastolic cardiac arrest and initial hypothermia. Typically, an initial dose of cardioplegia of 10 mL/kg was administered and supplemented with additional doses until a myocardial septal temperature of less than 15°C was achieved. After diastolic arrest, myocardial hypothermia was maintained with topical myocardial cooling. All distal coronary anastomoses were performed during one period of aortic occlusion using magnification and continuously placed 7-0 polypropylene sutures. Proximal anastomoses were completed with continuously placed 6-0 polypropylene sutures. Our preference was to use one or both of the IMAs and the greater or lesser saphenous veins in all patients if feasible when a vein graft was necessary. If the saphenous vein was found to be unacceptable on exploration at both ankles and groins, CPV was considered as an alternative conduit. The CPVs were implanted using the same technique and in the same sequence as for autologous saphenous vein. Samples of the CPV were sent for bacteriological and histological evaluation.

Allograft Vein Processing

All cryopreserved saphenous veins were obtained from CryoLife Cardiovascular Inc, Marietta, GA. The allograft veins were harvested "en bloc" from young cadavers within 10 hours of cardiac asystole and immediately perfused with Dulbecco's modified Eagle medium (DMEM) and papaverine, placed on ice, and shipped to CryoLife for processing. They were serologically screened and mounted on irrigating cannulas, and the branches were suture ligated. Next, they were placed in antibiotic solution and frozen at a controlled rate in a cryopreservation solution containing 10% dimethylsulfoxide, 10% fetal calf serum, 80% DMEM, and proprietary extracellular cryoprotectants. The veins were then stored in liquid nitrogen at −196°C.

Preparation of the Cryopreserved Veins

When a CPV was required, an ABO-matched vein of sufficient length was selected from the liquid nitrogen cryopreservation chamber and transported to the operating room in a special ice-cooled container. The CPV was then thawed and prepared according to the recommended protocol. The vein was then diluted, which consisted of immersing the vein for 5 minutes in each of three baths of dilution solution. The first bath contained DMEM with low levels of glucose, glutamine, hydroxy ethyl piperazine ethane sulfonic acid (HEPES) buffer, and mannitol. The third bath contained DMEM with low levels of glucose, glutamine, and HEPES buffer. The second bath contained a combination of the solutions in the first and third bath. During this process the vein was intermittently flushed with each solution. A swab of the CPV was sent for Gram stain before implantation. The vein was examined for damage and leaks were repaired with 7-0 polypropylene sutures. The CPV was flushed with heparinized saline solution immediately before implantation.

Postoperative Management

All patients were treated with aspirin starting upon arrival in the intensive care unit from the operating room. Patients were continued on aspirin therapy throughout their hospitalization and discharge. Selected patients were treated with dipyridamole depending on their cardiologist's preference. Patients with mechanical heart valves were treated with warfarin sodium. In these patients aspirin administration was frequently stopped at hospital discharge.

Patient Follow-up

All patients who received CPVs were scheduled to undergo either an ultrafast computed tomographic (CT) scan or cardiac catheterization postoperatively as part of the CPV implantation protocol. Clinical follow-up information was obtained by interview.

Ultrafast Computed Tomographic Scan Protocol

The patient's operative reports were reviewed to determine the number, placement, and type of aortocoronary bypass grafts. After an overnight fast, the patient was positioned in the supine position on the Imatron C-100 ultrafast CT scanner (Imatron Inc, San Francisco, CA). Electrocardiographic leads and intravenous access lines were placed. After a localization scan was performed to assure appropriate positioning, the scanner was programmed to obtain six axial slices of the chest.

A 40-mL dose of a nonionic contrast agent (Omnipaque 350; Winthrop Pharmaceuticals, New York, NY) was administered by a power injector at 10 mL/s for each flow study. Typically two flow studies were obtained for each patient. Imaging was begun 10 to 12 seconds after the intravenous infusion of dye for patients with normal left ventricular function and 15 to 30 seconds after injection for patients with impaired function. In each flow study 13 consecutive images were obtained, each triggered by the R wave of either every first or every second heartbeat (depending on the heart rate). This sequence accomplished contrast wash-in, peak concentration, and complete washout in most patients, and allowed for graft visualization and time-density analysis curves of the graft and aorta. Images were evaluated in a closed-loop movie mode and using time-density analysis. All CT scans were reviewed twice by one of us (W.J.E.). A graft was considered patent only if it was visualized on at least two scan levels in the distribution of the vessel bypassed.

Statistical Analysis

Data are reported as mean ± standard deviation. Fisher's exact test was used to compare patency rates between groups. The sign test was used to compare preoperative and postoperative function classification. A p value of less than 0.05 was considered to be statistically significant.

Results

All patients were hospital survivors. Fourteen patients were available for graft patency evaluation and made up the follow-up study group. Five patients could not be fully evaluated with either ultrafast CT scan or coronary angiography because 1 was out of the country, 2 refused follow-up, 1 had dye allergy, and 1 was claustrophobic to CT scan positioning. Graft patency analysis was performed with ultrafast CT scanning in 12 patients, and coronary angiography in 2. The follow-up period ranged from 2 to 16 months postoperatively (mean ± standard deviation, 7 ± 2 months). The group of patients who underwent graft patency analysis did not significantly differ from the total group of patients who underwent CPV implantation with regard to preoperative or operative descriptors.

The operative procedures, reason for CPV use, type of patency study, and individual graft patency results are shown in Table 1. The patients' age range was 55 to 76 years (mean ± standard deviation, 66 ± 7.2 years). Thirty-seven grafts were placed for an average of 2.64 grafts per patient (range, 1 to 4). All patients had the left IMA harvested, except 2 patients who had the left IMA used at a previous operation. At the time, we were conservative in our use of bilateral IMAs: 11 patients did not have bilateral IMAs used due to diabetes, advanced age, unsuitability, or deteriorating clinical status. The graft patency rates by conduit type were as follows: IMA, 93% (14 of 15 grafts); saphenous vein graft, 80% (4 of 5 grafts); and CPV, 41% (7 of 17 grafts). The patency of CPVs was significantly less than the patency rate for the autologous vessels (p[Fisher's exact test] = 0.004). The patient with an occluded left IMA had an occluded CPV and patent right IMA. At operation, the target vessel for the left IMA was thought to be of poor quality and size.

Ten patients had at least one occluded graft on follow-up. No predictor could be found for graft occlusion. Preoperative demographic descriptors and risk factors including age, sex, renal disease, pulmonary disease, history of hypertension, diabetes, liver disease, obesity, hypercholesterolemia, history of smoking, peripheral vascular disease, history of arrhythmia, congestive heart failure, history of angina, myocardial infarction, and previous cardiac or vascular operation did not correlate with graft occlusion. No correlation between target vessel site or size and patency was observed. We could not demonstrate any significant effect of treatment with aspirin, dipyridamole, or warfarin sodium on graft patency.

Complications included postoperative pump failure requiring open chest in 1, prolonged ventricular support in 2, and intraaortic balloon in 3 patients. Four patients had positive intraoperative bacteriologic cultures from a swab taken of the CPV at the time of implantation. All cultures grew coagulase-negative staphylococcus. Three of these patients were treated with prolonged courses of intravenous antibiotics. None of these patients had clinical evidence of mediastinal or systemic infection. Additionally, no correlation could be demonstrated between graft occlusion and positive CPV culture.

All patients showed functional improvement postoperatively (p[sign test] ≤ 0.001). This finding of an improvement in functional classification was also present in the subset of patients who had an occluded CPV. None of the patients had recurrence of angina postoperatively. One patient with two open CPV grafts had development of congestive heart failure secondary to unrecognized aortic stenosis, requiring reoperation 12 months postoperatively.

Comment

Currently the IMA and saphenous vein are the conduits of choice for coronary revascularization [1, 2]. However, there are situations in which the IMAs and saphenous veins are insufficient or unsuitable and alternative conduits may be necessary. The use of the gastroepiploic artery [11–13] and inferior epigastric arteries [14–17] has recently been advocated as a means of extending the range of conduits for autologous arterial revascularization. Despite excellent initial results, the long-term patency rates for these conduits have not been demonstrated. Additionally, all patients are not suitable candidates for the increased burden and complexity of these procedures.

Over the past two decades upper extremity veins, the radial artery, splenic artery, and synthetic grafts have all been evaluated as alternative conduits. However, each has demonstrated either suboptimal patency or limited applicability. Both the basilic and cephalic veins have been evaluated and have been found to have poor pa-

Table 1. Procedures and Graft Status

Patient No.	Operation	CPV Reason	Type of Patency Study	Interval to Follow-up (days)	Graft–Target Vessel	Graft Status
1	Reop CABG ×3	H, VV	UCT	476	LIMA–LAD SVG–OM CPV–distal LAD	Patent Patent Occluded
2	CABG ×3	H	UCT	396	LIMA–LAD SVG–RCA CPV–OM	Patent Occluded Occluded
3	CABG ×3	VV	Angio	135	LIMA–LAD CPV–OM2 CPV–PDA	Patent Patent Patent
4	CABG ×3	VV	UCT	55	LIMA–LAD CPV–RCA CPV–OM	Patent Patent Occluded
5	AVR, CABG ×2	H	UCT	262	LIMA–LAD CVP–RCA	Patent Patent
6	AVP, CABG ×2	H	UCT	113	LIMA–LAD CPV–OM	Patent Patent
7	Reop MVR, TVP, CABG ×1	H	UCT	305	CPV–LAD	Occluded
8	CABG ×3	UQ	UCT	250	LIMA–LAD SVG–PDA CPV–OM2	Patent Patent Occluded
9	Reop CABG ×2	UQ	UCT	210	CPV–LAD CPV–Diag2	Patent Occluded
10	CABG ×4	UQ	UCT	294	LIMA–LAD RIMA–AM SVG–RCA CPV–OM2	Patent Patent Patent Occluded
11	CABG ×3	UQ	Angio	82	LIMA–LAD RIMA–RCA CPV–OM1	Occluded Patent Occluded
12	CABG ×3	UQ	UCT	69	LIMA–LAD RIMA–RCA CPV–OM1	Patent Patent Patent
13	CABG ×3	VV	UCT	269	LIMA–LAD SVG–Diag CPV–RCA	Patent Patent Occluded
14	CABG ×2	H	UCT	203	LIMA–LAD CPV–OM	Patent Occluded

AM = acute marginal; Angio = coronary angiography; AVP = aortic valvuloplasty; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CPV = cryopreserved allograft vein; Diag = diagonal; H = previously harvested; LAD = left anterior descending; LIMA = left internal mammary artery; MVR = mitral valve replacement; OM = obtuse marginal; PDA = posterior descending artery; RCA = right coronary artery; Reop = reoperative; RIMA = right internal mammary artery; SVG = saphenous vein graft; TVP = tricuspid valve plication; UCT = ultrafast computed tomographic scan; UQ = unusable quality; VV = varicose veins.

tency rates and to dilate with time, and in addition they are more difficult to work with due to their thin, friable walls [1, 18, 19]. Although initial results with radial artery were satisfactory [20], several studies have demonstrated the development of severe concentric intimal hyperplasia and poor patency rates [21, 22]. The splenic artery has not gained popularity due to its limited range of applicability, difficulty to harvest, and predisposition to atherosclerotic changes [23, 24]. Synthetic conduits including Dacron [25] and polytetrafluoroethylene have been studied. Although sporadic case reports document patients with long-term patency, many studies have found unacceptably poor overall patency results [26–28].

In an effort to find an acceptable alternative conduit, several investigators have evaluated the use of allograft saphenous veins for coronary revascularization. Early results with fresh allograft saphenous veins as arterial bypass conduits have demonstrated poor patency results [4–6]. It has been speculated that the reason for failure was most likely due to immunologic mechanisms in these cases [29]. More recently cryopreservation has been attempted to decrease the immunologic response while preserving tissue structure and function [7, 9, 10]. However, studies of cryopreserved autologous saphenous vein for CABG have also shown poor patency. One criticism of these studies is that the vein preservation techniques used did not maintain cellular viability or structural integrity and probably resulted in frozen, but not preserved, veins. The role of tissue viability in graft patency is controversial; however, cellular viability is postulated to be responsible for the excellent results obtained with cryopreserved homograft aortic valves [30].

The techniques used to procure and cryopreserve the currently available allograft veins have been demonstrated to preserve endothelial cell viability, smooth muscle function, and structural integrity [9, 31] and thus could theoretically improve patency. This, in addition to the good initial clinical results as measured by patient survival and freedom from clinical symptoms of graft occlusion, encouraged us to reevaluate CPV as an alternative conduit. However, despite the advances in cryopreservation and good initial clinical results, we found CPV patency rates to be disappointing.

Although we used ABO cross-matching and antiplatelet agents, which may contribute to improved graft patency [29], our patency results were nevertheless suboptimal. There is some experimental evidence to suggest that cyclosporin can reduce the immunologic response to a CPV graft and may thus improve graft patency [10]. We chose not to use cyclosporin as this benefit has not been shown clinically, and the drug has potentially serious side effects.

This study emphasizes the need for patency follow-up in the evaluation of a new conduit. Although the patients did well clinically, the short-term graft patency was poor. In many conduit studies, patency follow-up with coronary angiography is difficult to obtain due to the risk, cost, and inconvenience of the procedure. Ultrafast CT scan is an appealing alternative because it correlates well with angiography [32] and is less expensive, minimally invasive, and more acceptable to the patient.

We conclude that the early patency rate for this CPV is significantly inferior to that of the autologous IMA and saphenous vein grafts. We believe that this patency rate of 41% for the CPV is unacceptable for most clinical situations. We recommend that CPV be used only when no other autologous conduit is available.

We thank Sandy Cassidy for her assistance with the preparation of the manuscript. We also thank Debbie Ilkowski, RN, for her help with chart review.

References

1. Foster ED, Kranc MAT. Alternative conduits for aortocoronary bypass grafting. Circulation 1989;79(Suppl 1):34–9.
2. Nishida H, Grooters RK, Soltanzadeh H, Thiemen KC, Schneider RF. Clinical alternative bypass conduits and methods for surgical coronary revascularization. Surg Gynecol Obstet 1991;172:161–74.
3. Green GE. Use of internal thoracic artery for coronary artery grafting. Circulation 1989;79(Suppl 1):30–3.
4. Bical O, Bachet J, Laurian C, et al. Aortocoronary bypass with homologous saphenous vein: long-term results. Ann Thorac Surg 1980;30:550–7.
5. Gelbfish J, Jacobowitz IJ, Rose DM, et al. Cryopreserved homologous saphenous vein: early and late patency in coronary artery bypass surgical procedures. Ann Thorac Surg 1986;42:70–3.
6. Tice DA, Zerbino VR, Isom OW, Cunningham JN, Engleman RN. Coronary artery bypass with freeze-preserved saphenous vein allografts. J Thorac Cardiovasc Surg 1976;71: 378–82.
7. Ladin DA, Lindenauer SM, Burkel WE, et al. Viability, immunologic reaction, and patency of cryopreserved venous allografts. Surg Forum 1982;33:460–3.
8. Sitzmann JV, Imbembo AL, Ricotta JJ, McManama GP, Hutchins GM. Dimethylsulfoxide-treated, cryopreserved venous allografts in the arterial and venous systems. Surgery 1984;95:154–9.
9. Brockbank EGM, Donovan TJ, Ruby ST, Carpenter JF, Hagen PO, Woodley MA. Functional analysis of cryopreserved veins: preliminary report. J Vasc Surg 1990;11:94–102.
10. Deaton DW, Stephens JK, Karp RB, et al. Evaluation of cryopreserved allograft venous conduit in dogs. J Thorac Cardiovasc Surg 1992;103:153–62.
11. Pym J, Brown PM, Charrette EJP, Parker JO, West RO. Gastroepiploic–coronary anastomosis: a viable alternative bypass graft. J Thorac Cardiovasc Surg 1987;94:256–9.
12. Verkkala K, Jarvinen A, Keto P, Kirtanen K, Lehtola A, Pellinon T. Right gastroepiploic artery as a coronary bypass graft. Ann Thorac Surg 1989;47:716–9.
13. Lytle BW, Cosgrove DM, Ratliff NB, Loop FD. Coronary artery bypass grafting with the right gastroepiploic artery. J Thorac Cardiovasc Surg 1989;97:826–31.
14. Vincent JG, van Son JAM, Skotnicki SH. Inferior epigastric artery as a conduit in myocardial revascularization: the alternative free arterial graft. Ann Thorac Surg 1990;49:323–5.
15. Puig LB, Ciongolli W, Cividanes GVL, et al. Inferior epigastric artery as a free graft for myocardial revascularization. J Thorac Cardiovasc Surg 1990;99:251–5.
16. Barner HB, Naunheim KS, Fiore AC, Fischer VW, Harris HH. Use of the inferior epigastric artery as a free graft for myocardial revascularization. Ann Thorac Surg 1991;52: 429–37.
17. Mills NL, Everson CT. Technique for use of the inferior epigastric artery as a coronary bypass graft. Ann Thorac Surg 1991;51:208–14.
18. Stoney WS, Alford WC, Burrus GB, et al. The fate of arm veins used for aorta–coronary bypass grafts. J Thorac Cardiovasc Surg 1984;88:522–6.
19. Schulman ML, Badhey MR. Late results and angiographic evaluation of arm veins as long bypass grafts. Surgery 1982;92:1032–41.
20. Carpentier A, Guermonprez JL, Deloche A, et al. The aorta to coronary radial artery bypass graft: a technique avoiding pathological changes in grafts. Ann Thorac Surg 1973;16: 111–21.
21. Curtis JJ, Stoney WS, Alford WC, et al. Intimal hyperplasia. A cause of radial artery bypass graft failure. Ann Thorac Surg 1975;20:628–35.
22. Fisk RL, Brooks CH, Callaghan JC, et al. Experience with the radial artery graft for coronary artery bypass. Ann Thorac Surg 1976;21:513–8.
23. Edwards WS, Lewis CE, Blakeley WR, et al. Coronary artery bypass with internal mammary and splenic artery grafts. Ann Thorac Surg 1973;15:35–40.
24. Edwards WS, Blakeley WR, Lewis CE. Technique of coronary bypass with autologous arteries. J Thorac Cardiovasc Surg 1973;65:272–5.
25. Sauvage LR, Berger K, Wood SJ, et al. Successful use of the USCI-Sauvage filamentous vascular prosthesis in the right coronary artery of man. In: Sawyer PN, Kaplit MJ, eds, Vascular grafts. New York: Appleton-Century Crofts, 1978: 378–86.
26. Sapsford RN, Oakley GD, Talbot S. Early and late patency of expanded polytetrafluoroethylene vascular grafts in aorta–coronary bypass. J Thorac Cardiovasc Surg 1981;81:860–4.
27. Hehrlein FW, Schlepper M, Loskot F, Scheld HH, Walter P, Mulch J. The use of expanded polytetrafluoroethylene (PTFE) grafts for myocardial revascularization. J Cardiovasc Surg 1984;25:549–53.
28. Chard RB, Johnson DC, Nunn GR, Cartmill TB. Aorta–coronary bypass grafting with polytetrafluoroethylene conduits. J Thorac Cardiovasc Surg 1987;94:132–4.
29. Ochsner JL, Lawson JD, Eskind SJ, Mills NL, DeCamp PT.

Homologous veins as an arterial substitute: long-term results. J Vasc Surg 1984;1:306–13.

30. O'Brien MF, Strafford EG, Gardner MAH, Pohlner PG, McGiffin DC. A comparison of aortic valve replacement with viable cryopreserved and fresh allograft valves, with a note on chromosomal studies. J Thorac Cardiovasc Surg 1987;94:812–23.
31. Brockbank KGM, Bank HL, Schmehl M. Ischemia and saphenous vein endothelial integrity. Transplant Proc 1989;21:1384–8.
32. Stanford W, Brundage BH, MacMillan R, et al. Sensitivity and specificity of assessing coronary bypass graft patency with ultrafast computed tomography: results of a multicenter study. J Am Coll Cardiol 1988;12:1–7.

DISCUSSION

DR FRITZ DEROM (Gent, Belgium): To evaluate how to obtain the best results with venous homografts, one of my associates, Dr Vermassen, did some research in dogs regarding preservation and postimplantation treatment. A total of 230 arterial reconstructions were performed. Five different preservation protocols and three postimplantation treatment protocols were compared.

Fresh autografts had a patency of 100%. Cryopreservation in Hanks' solution with 15% DMSO at −160°C gave nearly similar results. Autografts preserved in saline solution at 4°C and at −70°C or in glutaraldehyde solution were no better than synthetic grafts.

The results with viable, fresh or cryopreserved allografts were significantly worse than with the autografts. Histological as well as immunological evidence exists that rejection was the responsible mechanism for these occlusions.

Therefore we investigated whether immunosuppressive treatment could improve the results. We saw that treatment with cyclosporine (4 mg/kg per day) did indeed improve the patency to a level significantly better than after implantation of a synthetic graft or an untreated allograft.

A few patients were treated for distal peripheral vascular disease according to this protocol. The results are excellent but the follow-up is yet too short.

My question is: did you consider immunologic treatment in your patients?

DR LAUB: We have no experience with the use of immunologic modifiers in our patients. However, we are concerned with the long-term implications of immunosuppressive treatment in this patient population. We thank you for your information, which may be an important avenue for improving graft patency.

DR RAYMOND O. HEIMBECKER (Collingwood, Ont, Canada): Dr Laub and associates are to be congratulated on a very nice and much needed study. Now for a bit of ancient history: Beginning in 1956 Gordon Murray and I (this is prepump era) implanted fresh aseptic aortic homograft valves into the thoracic aorta of a series of patients with aortic insufficiency. The long-term success is well shown by selective angiography 15 years postoperatively, in which normal cusps, excellent function, and adjacent aortic wall calcification can be seen. Perhaps Dr Laub and associates would have a comment as to why the fresh aortic valve tissue fares so much better than cryopreserved veins.

DR LAUB: The long-term results you have obtained with aortic homograft valves are commendable. We believe the main reason why the performance of aortic valve tissue is superior to veins is the difference in their composition. The fibrous structure of the valve is weakly antigenic in comparison with the endothelium of the vein.

DR CRAIG R. SMITH (New York, NY): I enjoyed this report. I have a smaller experience in 8 patients, similar in every respect to yours. In the 2 patients who have been restudied, both cryopreserved veins were occluded. All the mammary arteries and saphenous veins were patent. So I have similar reluctance to be enthusiastic about it.

You did not mention something we have encountered in 2 patients who had remarkable pericardial effusions for many weeks postoperatively.

DR LAUB: We did not observe any postoperative pericardial effusions. However, we did observe a persistent left plural effusion in a patient in whom the left internal mammary artery was used. This patient's two cryopreserved grafts were patent.

DR KENNETH H. OBERHEU (Dayton, OH): In the early 1970s, we had a general surgeon who cooperated with us, and as he was taking our varicose veins across the hallway, he would not strip the vein the entire way. He would take the proximal vein out under direct dissection. This proximal portion was frequently suitable for bypass grafting. We took these portions of vein directly from one operating room across the way, and 8 or 10 years later had patients with patent grafts. I suggest that we look at family members of the same blood typing and use donor veins. We believe the fresh grafts are probably the key to patency.

DR LAUB: Previous results with fresh homograft transplants have been disappointing. It has been postulated that cryopreservation may ameliorate some of the immunogenicity of the transplanted tissue, and thus cryopreserved grafts may be preferable to fresh tissue.

Late Results of Operation for Ventricular Tachycardia

Lynda L. Mickleborough, MD, Shun-ichi Mizuno, MD, Eugene Downar, MD, and Gordon C. Gray, BSc

Division of Cardiovascular Surgery, Department of Surgery, and Division of Cardiology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

We have analyzed results in 54 consecutive patients with recurrent ventricular tachycardia and coronary artery disease in whom we used an aggressive surgical approach involving map-directed ventricular tachycardia ablation, scar excision and left ventricular remodeling, and coronary artery bypass grafting, as well as staged mitral valve replacement when necessary. We have previously shown age greater than 65 years to be an independent predictor of mortality and have excluded such patients from this series. Average age was 56 ± 7 years. All patients had a previous myocardial infarction; 24% of the infarctions (13/54) were posterior in location. Symptoms included syncope or presyncope in 83% of the patients (45/54), angina in 54% (29/54), and congestive heart failure in 52% (28/54). Extensive coronary artery disease was found in 78% (42/54), and 89% (48/54) had serious compromise of left ventricular function (ejection fraction <0.40; average ejection fraction, 0.28 ± 0.12). Only 63% (34/54) appeared to have a resectable left ventricular aneurysm on the preoperative angiogram. Ablation techniques included endocardial excision in 82% (44/54), with the addition of cryoablation in 60% (32/54), and balloon electric shock ablation in 22% (12/54); coronary artery bypass grafting was performed in 85% (46/54). There were four hospital deaths (7%). The surgical cure rate (no inducible VT at postoperative electrophysiologic study was 72% (39/54). During follow-up (mean, 50 ± 31 months) there have been six late deaths (1 sudden death, 1 stroke, 4 congestive heart failures with or without mitral regurgitation). Four patients with progressive congestive heart failure and serious mitral regurgitation have undergone repeat operation for mitral valve replacement. All are alive and doing well. Patient follow-up extends to 8 years, and actuarial survival is 79% with 97% freedom from sudden death. We conclude that an aggressive surgical approach in patients with recurrent ventricular tachycardia, extensive coronary artery disease, and poor left ventricular function yields excellent long-term results. During follow-up, reoperation for mitral valve replacement may be necessary in patients with progressive congestive heart failure associated with mitral regurgitation.

(Ann Thorac Surg 1992;54:832–9)

Many patients with recurrent ventricular tachycardia and coronary artery disease have had previous myocardial infarction and serious compromise of left ventricular function [1–3]. The treatment for such patients is controversial. In some centers, poor left ventricular function in the absence of a clearly resectable and localized aneurysm is considered to be a relative contraindication for surgical therapy [1, 2, 4], and these patients would be referred for implantation of an automatic implantable cardioverter defibrillator (AICD) with or without bypass grafting. We have taken a different approach in patients with ventricular tachycardia (VT) due to coronary artery disease who have dilated, poorly contracting left ventricles. In our series, even patients in whom only the basal constrictors are working are considered candidates for surgical cure of their VT (Fig 1). In all cases we have used an aggressive surgical approach involving map-directed ablation of the VT focus, scar excision and surgical left ventricular (LV) remodeling, and aortocoronary bypass grafting whenever possible, plus staged mitral valve replacement when necessary. We have reviewed our late results using this aggressive surgical approach.

Material and Methods

Patient Population

Patients were referred for operation because of (1) VT unresponsive to medical treatment, (2) intolerance to antiarrhythmic medications, or (3) other indications for operation, such as the presence of intractable congestive heart failure or ongoing angina with bypassable coronary artery disease. A global ejection fraction of less than 0.20 without a clearly resectable aneurysm (ie, a clearly demarcated area of akinesis or dyskinesis outside the expected boundaries of the contractile segments on ventriculogram) was not considered a contraindication for operation. Only if all walls were severely hypokinetic or if there was associated 3 to 4^+ mitral regurgitation were patients considered to have inoperable disease. We have previously shown that in our experience, advanced age is a

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Mickleborough, The Toronto Hospital, EN 13-217, 200 Elizabeth St, Toronto, Ont, Canada M5G 2C4.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

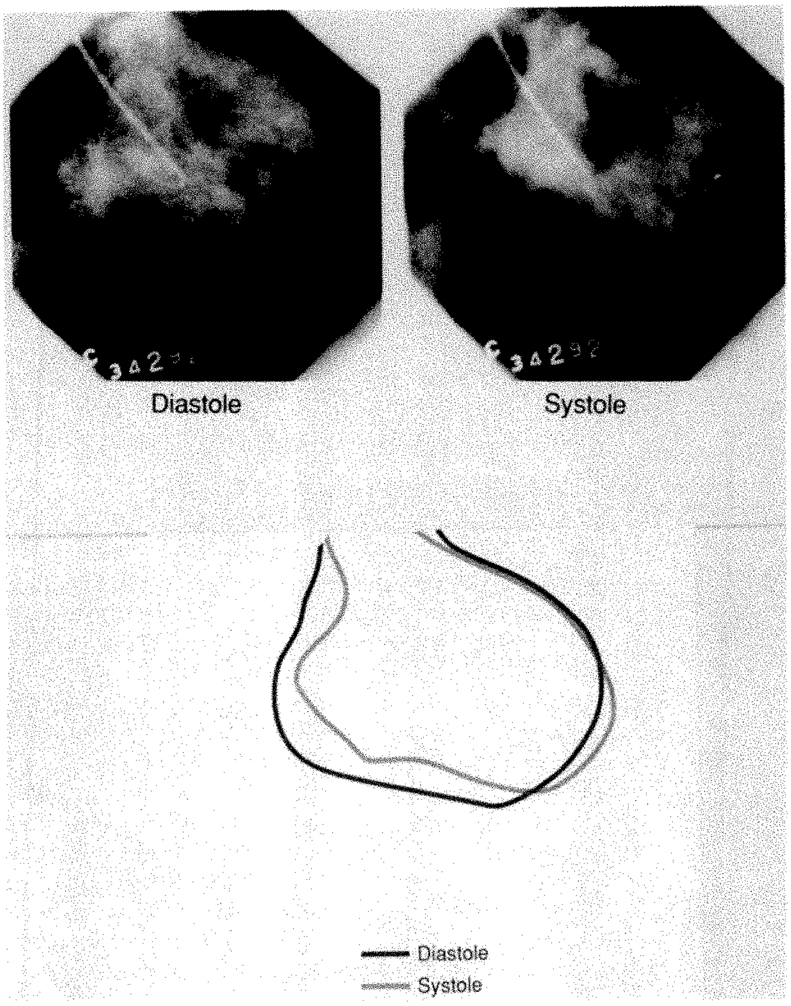


Fig 1. Representative diastolic and systolic frames from ventriculogram of typical patient undergoing left ventricular remodeling.

strong independent predictor of increased operative mortality with map-directed operation [5], and we have excluded 17 such patients (age >65 years) from this study. We have prospectively collected data on the remaining 54 consecutive patients in our VT surgical series operated on between August 1982 and June 1991.

There were 48 male and 6 female patients. The average age was 56 ± 7 years. All patients had had a previous myocardial infarction, and 9% (5/54) were operated on within 3 months of an acute infarct. Infarcts were anteroapical in 41 patients and posterior in 13 (24%). Presenting symptoms included syncope in 69% (37/54), presyncope in 15% (8/54), angina in 54% (29/54), and congestive heart failure in 52% (28/54). All patients had been receiving a number of antiarrhythmic medications before operation, with an average of 3.8 ± 1.8 drugs per patient. In 30 patients (57%) who were receiving amiodarone, administration of the drug was stopped for at least 2 weeks before operation. Extensive coronary artery disease (involving 2 to 3 major vessel distributions) was present in 78% (42/54). Serious compromise of LV function, defined as an ejection fraction less than 0.40, was present in 48 patients (89%); 20 patients (37%) had grade III ventricle, and 28 (52%) had grade IV ventricle. Average ejection fraction for the entire group was 0.28 ± 0.12. On the preoperative angiogram there appeared to be a clearly demarcated area of akinesis or dyskinesis (LV aneurysm) in 34 patients (63%).

Intraoperative Technique of Mapping

All patients had epicardial and endocardial LV mapping. Since December 1984 we have used the transatrial balloon technique and on-line video display system previously described [6] to obtain simultaneous epicardial and LV endocardial activation maps. When a right ventricular or septal site of origin was suspected based on the timing of epicardial versus LV endocardial activation, an additional right ventricular balloon was used in 3 patients (5%). In this series we did not encounter any tachycardia that appeared to be originating in the epicardial or subepicardial layers. As previously described the patterns of activation observed were classified as monoregional, figure of 8, or circular, and the target areas were chosen on the basis of the earliest site of activation plus the location of suspected reentry pathways [6]. Once mapping had been completed and all target areas had been chosen, specific electrode locations on the ventricular balloon were identified for ablation.

Ablation Techniques

The surgical approach depended on the location of target areas and the extent and distribution of previous scarring in the ventricle. In most patients an area of previous infarction was easily identifiable and the ventricle was opened in this region whether or not there was evidence of transmural scarring. After exposure and visual orientation of the balloon, endocardial excision was carried out in the target areas indicated by mapping. When the target areas involved deep layers of the septum or areas of papillary muscle insertion, deeper ablation was achieved with subsequent application of the cryoprobe. In patients in whom a localized infarct could not be identified, on the basis of either a wall motion abnormality or the presence of epicardial scarring, we attempted to ablate the VT focus by passing electric current through target beads on the mapping balloon in the intact ventricle (a technique that we call balloon electric shock ablation) [5]. After shock delivery, attempts were made to reinduce the arrhythmia. If ventricular tachycardia could still be induced, an apical ventriculotomy incision was performed and endocardial excision with or without cryoablation was carried out.

Techniques of Scar Excision and Left Ventricular Remodeling

In patients with what appeared to be an aneurysm on the angiogram, the akinetic or dyskinetic area was excised. The resected specimens often contained a substantial amount of viable muscle mixed with scar. Simple linear closure was employed in all but 3 of these patients, in whom heavy calcification within the remaining wall required patch closure of the defect. In patients without an aneurysm, a ventriculotomy was made in the area of previous infarction through a mixture of viable muscle and scar, and resection of the hypokinetic wall (as identified in the beating heart) was carried out so as to restore left ventricular geometry and shape to as near normal as possible. The suture line in these patients often encompassed thick portions of the wall. We call this procedure LV surgical remodeling. In these cases, the defect was also tailored to allow simple linear closure. In addition, aortocoronary bypass grafting was performed when indicated. The proximal left anterior descending artery was grafted whenever possible even if the vessel had been amputated in the repair (24%).

Postoperative Electrophysiologic Study

An electrophysiologic study was performed 2 weeks postoperatively with pacing from multiple sites in the right ventricle. The protocol included pacing at two basic cycle lengths with up to three premature extra stimuli and burst pacing to a basic cycle length of 250 milliseconds. Pacing was continued until completion of the protocol or initiation of sustained VT (>30 seconds).

Statistical Analysis

Statistical analysis was performed using the Statistical Analysis System program (SAS Institute Inc, Cary, NC). Values for continuous variables are expressed as mean ± standard deviation. Kaplan-Meyer actuarial curves for survival and freedom from sudden death were constructed. Differences between age groups were evaluated by χ^2 statistics for discrete variables and Student's t test for continuous variables.

Results

Intraoperative Inducibility of Arrhythmias

With the transatrial balloon inflated we were easily able to induce and map multiple runs of VT in 100% of the patients. Activations maps of more than one morphology were obtained in 39 of 54 (72%), with an average of 2.6 ± 1.3 morphologies mapped per patient (range, 1 to 8).

Details of Operative Intervention

Transmural scarring allowed a conventional left ventricular aneurysm resection in 26 patients (48%). Removal of wall that contained a substantial amount of viable muscle mixed with scar or LV remodeling was carried out in 20 patients (37%). Balloon electric shock ablation was attempted in 12 patients but was unsuccessful in 4. These patients were then treated with endocardial excision or cryoablation. Ablation techniques included endocardial excision in 82%, cryoablation in 60%, and balloon electric shock ablation in 22%. In spite of detailed intraoperative mapping, the extent of endocardial excision was quite large, with an average of 30 ± 20 cm^2 resected per patient. Aortocoronary bypass grafting was performed in 85% of patients, with an average of 2.3 ± 0.8 grafts per patient. Because mapping and LV remodeling were performed on the open beating ventricle, the cross-clamp or ischemic time was limited (average, 71 ± 30 minutes) compared with the cardiopulmonary bypass time (average, 247 ± 48 minutes).

Morbidity and Mortality

Ninety-three percent of patients survived the operation and were discharged from the hospital. In the perioperative period, inotropic and intraaortic balloon support were required in 72% and 22% of patients. There were four hospital deaths, all in patients who had received amiodarone within 1 month of operation. Three patients died of congestive heart failure, 1 with associated recurrent ventricular arrhythmias. The fourth patient died of fulminant bronchopneumonia on the fifth postoperative day.

At the postoperative electrophysiologic study, inducible VT of any morphology was considered clinically significant. Only 11 patients had inducible VT, corresponding with a surgical cure rate in this series of 72%. The patients with inducible arrhythmias were empirically treated with amiodarone and discharged with further follow-up including office visits and Holter monitoring.

Follow-up ranges from 6 months to 8 years (average, 50 ± 31 months). There have been six late deaths in this series. Chest pain suddenly developed 2 years postoperatively in 1 patient, who died before he could reach medical attention (sudden death). His postoperative electrophysiologic study had been negative and he had been

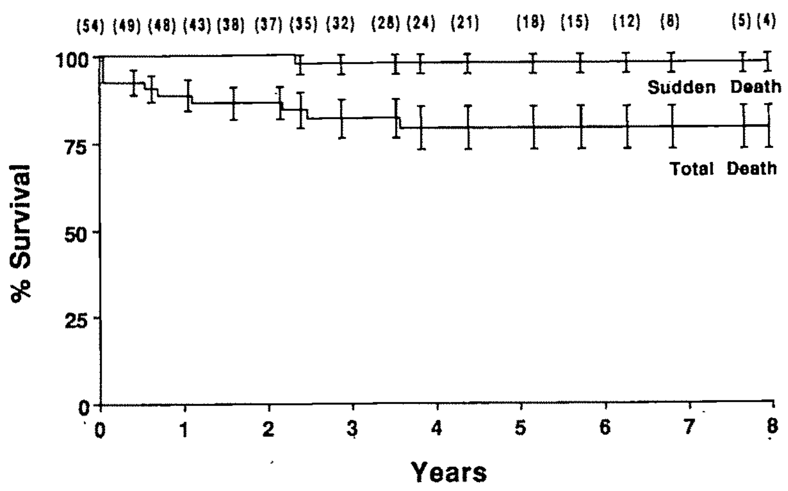


Fig 2. Actuarial curve for postoperative survival and freedom from sudden death. The percent of patients surviving after operation is plotted against time. Standard errors of the mean are indicated by the vertical bars. Numbers in parentheses indicate the number of patients remaining in follow-up at the beginning of each time interval.

receiving no antiarrhythmic medications and had had no evidence of recurrent arrhythmias. A second patient died of a stroke. The remaining four late deaths were due to progressive congestive heart failure. In 3 of these patients, serious mitral regurgitation had been identified and vigorous medical management instituted. Unfortunately these patients were not considered candidates for mitral valve replacement, and all died within 1 year of the original operation. This prompted us to consider mitral valve replacement as a salvage procedure in 4 similar patients who, during follow-up, had increasing symptoms of congestive heart failure and were found to have serious mitral regurgitation. These 4 have undergone successful mitral valve replacement and are alive and doing well. These results would seem to contradict conventional wisdom, which predicts a dismal outcome if a valve prosthesis is inserted for mitral regurgitation in the face of severe compromise of LV function. Timing of the second operative procedure in these 4 patients was 10 months in 3 patients and 14 months after the initial operation in 1 patient. Two further patients in this series have undergone cardiac transplantation because of progressive congestive heart failure, one 15 months and one 3 years 2 months after the initial operation. These patients are also alive and doing well.

Follow-up in the remaining 43 patients extends to 8 years. The actuarial survival is 79%, with 97% freedom from sudden death (Fig 2).

Comment

For patients with coronary artery disease and recurrent VT, therapeutic options for control of the arrhythmia include drug therapy, map-directed operation, catheter ablation of VT foci, or implantation of an AICD. To choose the most appropriate therapy for an individual patient, the relative risks and benefits of each approach must be examined.

In our map-directed surgical series, the single most important predictor of operative mortality and poor long-term results by multivariant analysis has been age greater than 65 years. Excluded from this report were 17 patients older than 65 years (average age, 70 ± 3 years) whose clinical and intraoperative variables are summarized in Table 1. More patients in the older group had posterior infarcts (35% versus 24%) and were receiving amiodarone at the time of operation (71% versus 57%), but these

Table 1. Preoperative, Intraoperative, and Postoperative Variables in Patient Population Aged Greater Than 65 Years ($n = 17$)

Variable	Value[a]
Age (y)	70 ± 3.0[b]
Sex (M/F)	16/1
Previous myocardial infarction	100 (17/17)
Posterior location	35 (6/17)
Amiodarone at time of operation	71 (12/17)
LV aneurysm (preop angiogram)	53 (9/17)
Double/triple-vessel disease	88 (15/17)
Grade III ventricle	35 (6/17)
Grade IV ventricle	47 (8/17)
Ejection fraction	0.27 ± 0.20
Multiple morphologies mapped	53 (9/17)
No. of morphologies mapped	2.6 ± 1.3
Aneurysm resection	53 (9/17)
LV remodeling	29 (5/17)
Endocardial excision	71 (12/17)
Cryoablation	59 (10/17)
Balloon electric shock ablation	24 (4/17)
Coronary artery bypass grafting	88 (15/17)
Cross-clamp time (min)	69 ± 32
Pump time (min)	264 ± 56
Intraaortic balloon pump	35 (6/17)
Dopamine required	94 (16/17)
Hospital survival	65 (11/17)[b]
Negative postop electrophysiologic study	41 (7/17)[b]
Late sudden death	6 (1/17)
Total late deaths	29 (5/17)

[a] Values are shown as percentage with number of patients in parentheses or as mean ± standard deviation as applicable. [b] Different from younger age group; $p < 0.05$ by χ^2 statistics or t test.

LV = left ventricular.

trends did not reach statistical significance. At operation similar procedures were carried out in the greater than 65-year age group, and there was no difference in the percentage of patients receiving bypass grafts, the average number of grafts performed, or the average cross-clamp or pump time. In the older patients the hospital mortality was 35% as compared with 7% in the younger group ($p < 0.05$). More elderly patients required inotropes in the postoperative period (94% versus 72%), but this difference was not statistically significant. In the older group results related to arrhythmia control were not as good, with only a 41% cure rate versus 72% in the younger patients ($p < 0.05$). During follow-up in the elderly, the incidence of sudden death was 12% versus 2% and the total mortality was 29% versus 11%. Based on these results we decided not to perform map-directed VT operation in patients more than 65 years of age [5] unless they have ideal anatomy with a clearly resectable aneurysm, relatively well preserved ventricular function, and good vessels for bypass grafting.

In patients with VT and coronary artery disease the arrhythmia is only one manifestation of a complex problem. In our experience, these patients have in addition to their electrical instability increased risks related to underlying poor LV function, with or without mitral insufficiency, and the potential for recurrent ischemic episodes. In such patients the optimal treatment would prevent the arrhythmia, reverse the ischemia, and restore left ventricular geometry and shape toward normal as much as possible.

In assessing patients for operation, the angiographic appearance can be misleading. In some patients who appeared to have an aneurysm on the ventriculogram, we failed to find a thinned out area of scar at the time of operation. In these and other patients who had no localized wall motion abnormality, the ventriculotomy incision required to gain access for endocardial ablation was made through a mixture of viable muscle and scar. Surgical ventricular remodeling was then performed with excision of a portion of the wall, so that primary closure of the defect resulted in reduction of LV size and restoration of ventricular geometry toward normal as much as possible.

In this series of patients with extensive coronary artery disease and poor LV function, map-directed operation was accomplished with a hospital mortality of only 7%. In addition we have achieved an 8-year survival of 79%. These figures compare quite favorably with those from other reported series of map-directed operation or AICD implantation. Hargrove and associates [1] reported a 4-year survival of only 60% after map-directed endocardial excision or AICD implantation with or without aortocoronary bypass grafting. Elefteriades and co-workers [2] reported a 10% operative mortality when AICD implantation was combined with aortocoronary bypass grafting, and the 2-year survival in their series was only 72%. Fogoros and colleagues [7] reported a 3-year survival of only 67% after AICD implantation in patients with coronary artery disease and a poor ejection fraction (<0.30). The patients entered into these series are not strictly comparable with those in our series because of differences in age and the proportion of patients with coronary artery disease and poor left ventricular function; therefore, it is difficult to make conclusions regarding efficacy of various therapies.

In our series 11 patients had inducible VT postoperatively. Three of these patients had posterior infarcts and 5 had been receiving amiodarone at the time of operation. Seven of these patients had multiple VT morphologies with up to five different VTs mapped at the time of operation. The operative technique varied in these cases. Six patients underwent a left ventricular aneurysm resection, 2 underwent LV remodeling, and 1 patient was treated with balloon electric shock ablation. During follow-up (mean follow-up, 4 years 9 months) 6 of these patients are alive and well controlled on low-dose amiodarone (1 g/wk). One patient has required a mitral valve replacement and is now doing well 1½ years after the original operation. One patient is on the waiting list for cardiac transplantation because of severe congestive heart failure 2 years after the original operation. Three patients have died of congestive heart failure without clinical recurrence of their arrhythmias (1 year, 3 years 5 months, and 8 years 9 months after the original operation). We have treated our surgical failures with low-dose amiodarone because we believed that it was the most effective antiarrhythmic medication available and have been gratified with our results. There have been no late sudden deaths in this group. Of course toxicity of the drug may become an important problem in these patients in the long term.

Long-term follow-up in most AICD series (with or without coronary artery bypass grafting) has shown that late deaths are not due to arrhythmias but rather to progressive congestive heart failure. Whether the increasing failure is due to repeated ischemic events or ongoing changes in LV dilatation and geometry that are not prevented or corrected by insertion of the AICD has not been determined. In our series, the beneficial effects of an aggressive surgical approach are probably due to a combination of revascularization (including the proximal left anterior descending artery whenever possible) and scar excision and LV remodeling in addition to effective arrhythmia control. Possible benefits of LV remodeling that brings the size and shape of the ventricle back toward normal as much as possible could include decreased wall stress, decreased oxygen consumption, and improved fiber orientation in the remaining myocardium, which might result in increased contractility in these regions of the heart [8–11].

We believe that the relationship between poor LV function, chamber dilatation, and mitral valve function is a complex one. Early in our experience clear signs of mitral regurgitation developed in 1 patient within 6 months of the mapping procedure. We wondered if this could be a complication of the transatrial balloon mapping technique or of the ablation procedure (balloon electric shock ablation, endocardial excision, or cryoablation) when preformed close to the papillary muscle insertion. To assess possible negative effects of the operative procedure on mitral valve function, we began performing

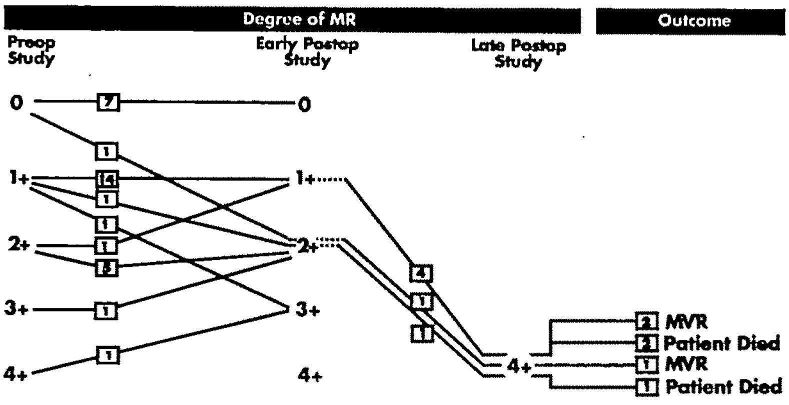


Fig 3. Results of preoperative and early and late postoperative Doppler echocardiographic assessment in patients undergoing map-directed ventricular tachycardia operation. Mitral regurgitation (MR) has been graded on a scale of 1^+ *to* 4^+*. Only patients in whom severe congestive heart failure has developed have undergone a late echocardiographic follow-up study. (MVR = mitral valve replacement.)*

preoperative and postoperative Doppler echocardiographic examinations to prospectively assess the presence and severity of mitral regurgitation in all patients. The postoperative study was performed 10 days to 2 weeks after the mapping procedure. Results of these studies are given in Figure 3.

The preoperative studies have shown that in patients with poor LV function, angiography often underestimates the degree of mitral regurgitation as assessed by echocardiographic techniques. We have relied on our Doppler echocardiographic data to make decisions with regard to operability. If on the preoperative echocardiographic study 4^+ mitral regurgitation is present in the setting of severe global LV dysfunction (ejection fraction <0.20), we would not consider the patient a candidate for map-directed operation. If mitral regurgitation is mild to moderate (2 to 3^+) or if 4^+ regurgitation is believed to be due to acute ischemic or arrhythmic events, we would proceed with operation. In such patients we were reluctant to replace the mitral valve for fear that this might accentuate the degree of LV failure and hoped that revascularization and remodeling would improve mitral valve function. Also we were reluctant to prolong the complex mapping procedure for the time necessary to perform a valve replacement. As shown in Figure 3, in 21 patients assessed by Doppler echocardiography, there was no serious mitral regurgitation on either the preoperative or postoperative study. In 8 patients who had serious preoperative mitral regurgitation (2^+ or greater), the regurgitation was either unchanged (in 5) or improved (in 3) postoperatively. Thus in 29 of 32 patients (91%) studied with preoperative and postoperative echocardiography, the operative procedure did not appear to have a negative effect on mitral valve function. In only 3 patients was there evidence of increased mitral regurgitation on the early postoperative study. In 1 patient the degree of mitral regurgitation increased from 1^+ to 3^+. This patient has been successfully managed with medical therapy. In 2 other patients in whom mitral regurgitation increased from 0 to 2^+ and from 1^+ to 2^+ there has been progression of symptoms with time. One of these patients had undergone a successful mitral valve replacement and the other died of severe congestive heart failure.

In our overall series symptoms of progressive congestive heart failure associated with severe mitral regurgitation have developed in a total of 7 patients late after the mapping procedure. In this subgroup the original procedure performed was LV resection in 3, LV remodeling in 2, and balloon electric shock ablation in 2. Although conventional thinking would suggest that mitral valve replacement would have little role to play in this setting of poor LV function, we have successfully performed mitral valve replacement as a salvage procedure in 4 of these patients. These patients have been followed up for 5 months, 2 years 9 months, 3 years 6 months, and 5 years 3 months after the mitral valve replacement. All 4 are alive and have experienced marked improvement of symptoms. In 1 of these patients, symptoms of severe congestive heart failure were intermittent and difficult to understand. At catheterization, initially there was no evidence of a mitral valve problem, but with injection of a small amount of dye, florid mitral regurgitation developed and the patient went acutely into pulmonary edema. In this patient, with very poor LV function and end-stage ischemic cardiomyopathy, mitral regurgitation appeared to be highly dependent on preload and afterload. This patient had substantial improvement in her symptoms after mitral valve replacement.

The other 3 patients in whom congestive heart failure and mitral regurgitation developed were not referred for consideration of mitral valve replacement, and all have died of intractable failure. These cases illustrate that after map-directed operation patients must be rigorously assessed, not only for recurrent arrhythmias, but for increasing heart failure and mitral regurgitation. In such patients our experience shows that poor LV function does not necessarily preclude good results after replacement of the mitral valve.

In conclusion, we believe that in patients with coronary artery disease, previous infarction, and poor LV function, VT may be just one manifestation of a complex disease process. In such patients, prevention of sudden death alone is not optimal management. Poor LV function with the lack of a clearly demarcated resectable aneurysm should not be considered a contraindication for map-directed operation. The decision whether to operate should not be made on the basis of global ejection fraction but requires careful assessment of the subjective appearance of the left ventricle. In these cases we have demonstrated that an aggressive surgical approach involving map-directed ablation of VT foci, scar excision, and LV remodeling, plus revascularization whenever possible, can be accomplished with a low operative mortality and good long-term results. Close follow-up of these patients with optimal medical treatment is mandatory. When symptoms of congestive heart failure that are resistant to medical management occur, even if they are intermittent, mitral regurgitation should be considered as a contributing factor and mitral valve replacement should be offered as a therapeutic option.

Supported in part by a grant from The Heart and Stroke Foundation of Ontario.

We extend our appreciation to Ms Hilary Vincent for the excellent preparation of the manuscript.

References

1. Hargrove WC III, Josephson ME, Marchlinski FE, Miller JM. Surgical decisions in the management of sudden cardiac death and malignant ventricular arrhythmias: subendocardial resection, the automatic internal defibrillator or both. J Thorac Cardiovasc Surg 1989;97:923–8.
2. Elefteriades JA, Biblo LA, Batsford WP, et al. Evolving patterns in the surgical treatment of malignant ventricular tachyarrhythmias. Ann Thorac Surg 1990;49:94–100.
3. Swerdlow CD, Winkle RA, Mason JW. Determinants of survival in patients with ventricular tachyarrhythmias. N Engl J Med 1983;308:1436–42.
4. Cox JL. Patient selection criteria and results of surgery for refractory ischemic ventricular tachycardia. Circulation 1989; 79(Suppl 1):163–77.
5. Mickleborough LL, Usui A, Downar E, Harris L, Parson I, Gray G. Transatrial balloon technique for activation mapping during operations for recurrent ventricular tachycardia. J Thorac Cardiovasc Surg 1990;99:227–33.
6. Mickleborough LL, Harris L, Downar E, Parson I, Gray G. A new intraoperative approach for endocardial mapping of ventricular tachycardia. J Thorac Cardiovasc Surg 1988;95: 271–80.
7. Fogoros RN, Elson JJ, Bonnet CA, Fiedler SB, Burkholder JA. Efficacy of the automatic implantable cardioverter-defibrillator in prolonging survival in patients with severe underlying cardiac disease. J Am Coll Cardiol 1990;16:381–6.
8. Nicolosi A, Spotnitz HM. Quantitative analysis of regional systolic function with left ventricular aneurysm. Circulation 1988;78:856–62.
9. Louagie Y, Alouini T, Lesperance J, Pelletier LC. Left ventricular aneurysm with predominating congestive heart failure: a comparative study of medical and surgical treatment. J Thorac Cardiovasc Surg 1987;94:571–81.
10. Dymond DS, Stephens JD, Stone DL, Elliott AT, Rees GM, Spurrell RAJ. Combined exercise radionuclide and hemodynamic evaluation of left ventricular aneurysmectomy. Am Heart J 1982;104:977–87.
11. Jatene AD. Left ventricular aneurysmectomy: resection or reconstruction? J Thorac Cardiovasc Surg 1985;89:321–31.

DISCUSSION

DR JAMES E. LOWE (Durham, NC): Dr Mickleborough's group is to be congratulated for achieving excellent results in a very heterogenous and high-risk group of patients with medically refractory VT who underwent endocardial map-guided VT ablative procedures. The report raises a number of very interesting questions.

There appear to be three different treatment groups. One group underwent LV aneurysm resection and repair with a concomitant VT ablative procedure. Approximately 22%, 12 of your 54 patients, underwent balloon shock therapy with 4 failures, who I assume crossed over into the original 8 of 54 patients, or 15%, who underwent LV scar revision and LV remodeling.

I have a number of questions. Could you specify for us the operative mortality, long-term survival, and freedom from VT without medication for each of these three different treatment groups? Next, what was the operative mortality and long-term survival and VT cure rate in the 18 patients greater than age 65 years whom you excluded from your present study? Do you presently reject all patients greater than age 65 years for VT map-directed operation? We have not found in our series that age greater than 65 years per se is associated with an increased operative mortality, especially in patients with well-defined LV aneurysms and inducible and mappable VT. In fact 25% of our patients are greater than 65 years of age and our operative mortality over the past 7 years has remained constant, at 8%.

Your surgical cure rate, 72%, is excellent. However, the 11 patients still inducible after operation were all empirically treated with postoperative amiodarone. How many of these 11 patients were receiving preoperative amiodarone, which was unsuccessful as you point out in your manuscript, in controlling their VT, and how many were controlled by postoperative amiodarone? What were the long-term side effects of chronic amiodarone treatment in these patients? How many patients with late death were receiving amiodarone? It is uncertain to me why postoperative electrophysiologic studies were not done before discharge on those 11 patients given amiodarone. Was any consideration given in this subgroup who were still inducible postoperatively to AICD implantation instead of amiodarone therapy? All operative deaths, interestingly, occurred in patients receiving preoperative amiodarone.

Dr Bill Buhrman in our electrophysiologic laboratory treated a colony of 10 dogs with oral amiodarone for 4 weeks, achieving midrange therapeutic levels based on high-performance liquid chromatography serum analyses, and 10 additional animals served as untreated controls. After this 4-week period of treatment all hearts were then subjected to aortic cross-clamping and 60 minutes of cold-potassium cardioplegic arrest followed by reperfusion. Graded infusions of epinephrine essentially had no effect on the developed pressure over time in the amiodarone-treated hearts, whereas the untreated control hearts behaved as you would expect, with increasing levels of epinephrine infusion resulting in a greater developed pressure over time.

These experimental data suggest to us that amiodarone renders hearts relatively catecholamine insensitive, and this may relate to the increased operative mortality in patients receiving amiodarone, because the majority have impaired LV function and would definitely benefit from postoperative inotropic support.

In summary, this is a very impressive update on your surgical series of VT patients. The data you have presented support your conclusion that poor LV function in the absence of a clearly defined LV aneurysm should not be considered an absolute contraindication for map-directed operation.

DR MICKLEBOROUGH: Dr Lowe, you asked so many questions I know I am going to miss some of them, but I will try my best. To clarify the first point, as stated in the presentation LV modeling was carried out in 37% of patients in this series, including the 4 patients who crossed over from the balloon electric shock ablation group, as you pointed out.

I cannot give you the actuarial survival statistics in the three subgroups (LV aneurysm resection, LV remodeling, and balloon electric shock ablation) but it is my impression, having looked at the data very carefully, that those patients with a resectable aneurysm do the best. By expanding the indications for map-directed operation and accepting patients who have globally poor LV function, you make things more difficult. To answer your specific questions, 3 of 4 hospital deaths occurred in the LV remodeling and balloon electric shock ablation groups. The long-term survival has not been as good in these patients as in those with a clearly resectable aneurysm. However, because of the small numbers involved, we do not have actuarial statistics for each of the subgroups. Patients with a clearly resectable aneurysm are excellent candidates for map-directed operation, and I believe that if you only do such cases, you should achieve a cure rate of 85% to 90% rather than the 72% reported in this series.

As to your question regarding map-directed operation in patients over the age of 65 years, I do not consider age alone to be an absolute contraindication. I have operated on several patients older than 65 years who had discrete aneurysms and who were otherwise excellent candidates. They all have done very well. However, in our experience the overall mortality in patients older than 65 years we have operated on with map-directed operation was 30%, and as a group these patients have been excluded from the series. At the present time I would only consider a patient more than 65 years old as a candidate for this type of operation if he or she had ideal anatomy; that is, a clearly resectable aneurysm.

There is no question that patients receiving amiodarone present a formidable challenge to any operative procedure, but especially one that involves long pump runs. I believe your observations in dogs given amiodarone with respect to response to catecholamines are correct. About 6 years ago we presented at another meeting our observations that several of our patients who had been receiving amiodarone at the time of operation exhibited an unusual syndrome postoperatively. They would have adequate cardiac outputs but very low peripheral vascular resistance and it was very hard to maintain a high enough perfusion pressure to keep their kidneys working. They did not respond in the usual manner to catecholamines or vasopressors and presented a considerable management challenge. Our group has also observed a higher incidence of pulmonary complications in patients who have been given amiodarone.

All of the patients who were discharged on a regimen of amiodarone in this series had had a positive postoperative electrophysiologic study. In the early years of our series we considered amiodarone to be the only reasonable option in these patients. During follow-up we were very impressed with the extremely low incidence of sudden death or symptomatic recurrence of arrhythmias. Because of this experience, we have not performed repeat electrophysiologic testing nor have we considered AICD implantation in patients unless there are clinical indications during follow-up. None of the patients in this series have needed AICDs.

I have been asked to summarize. In reporting results of therapy in patients with VT, it is important to look at freedom from sudden death and overall survival. We believe that we have achieved excellent results in this series even in patients with poor LV function and no clearly resectable aneurysm. We believe that the results in this series compare very favorably with those achieved with any other treatment modalities including AICD implantation with or without aortocoronary bypass grafting.

Thank you for the privilege of presenting these data.

Cardiac Retransplantation: A Viable Option?

Shreekanth V. Karwande, MD, R. Douglas Ensley, MD, Dale G. Renlund, MD,
William A. Gay, Jr, MD, Wayne E. Richenbacher, MD,
Donald B. Doty, MD, M. Elizabeth Hammond, MD, John D. Marks, PE, and
The Registry of the International Society for Heart and Lung Transplantation

Division of Cardiothoracic Surgery, University of Utah School of Medicine, and Utah Transplant Affiliated Hospitals Cardiac Transplant Program, Salt Lake City, Utah

To evaluate cardiac retransplantation as an appropriate utilization of scarce donor organs we analyzed data from the registry of the International Society for Heart and Lung Transplantation (ISHLT) (n = 449) and the Utah Cardiac Transplant Program (n = 20). Actuarial survival among retransplants was lower than in patients who received only one transplant in both the ISHLT registry patients (1 year survival, 48% versus 78%; $p = 0.001$) and the Utah series (1 year survival, 74% versus 88%; $p = 0.06$). Uncontrolled rejection, short interval (<6 months) between transplantations, and the need for mechanical circulatory support were identified as risk factors for retransplantation. The incidence of rejection and infection was similar in first and second transplant recipients. Second transplant recipients had a higher level of sensitization, a greater incidence of donor-specific positive crossmatches, and an increased early mortality. Repetition in the second donor of mismatched HLA antigens present in the first donor did not adversely affect survival. If patients who underwent retransplantation within 6 months of their initial transplantation, those receiving transplants for uncontrolled rejection, and those requiring mechanical assistance were eliminated from the study, the short-term and long-term survival after cardiac retransplantation does not differ from that in patients having a single transplant.

(Ann Thorac Surg 1992;54:840–5)

Since the first report of cardiac retransplantation in 1977, more than 400 such procedures have been reported to the registry of the International Society for Heart and Lung Transplantation (ISHLT) [1, 2]. The three principal causes of allograft failure leading to retransplantation are accelerated allograft coronary artery disease (ACAD), rejection, and nonspecific graft failure. In view of the acute shortage of donor organs we decided to examine cardiac retransplantation by using data from two sources.

All recipients of a second heart transplant reported to the ISHLT registry were compared with a matched group of first heart transplant recipients. Data for retransplantation recipients in the Utah Cardiac Transplant Program were collected to compare and contrast with the ISHLT data and to examine variables not covered by the registry data.

Material and Methods

ISHLT Registry Data

Between November 1968 and October 1991 the ISHLT registry received data for 449 recipients who underwent retransplantation worldwide. Data were also analyzed for an equal number of primary transplant recipients who were matched for transplant center, year of transplantation, age, and sex. Outcome variables examined included survival and cause of death. Potentially predictive variables examined were age, sex, cause of allograft failure, interval between first and second transplantation, immunosuppressive regimen, and experience of the transplant center.

Utah Cardiac Data

Between March 1985 and December 1991 420 cardiac transplantations were performed, 20 of which were second transplant procedures. Third transplant procedures required in 2 patients were not included in the analysis. All of the variables mentioned above, with the addition of HLA typing, donor-specific crossmatch, percent panel reactive antibody (PRA), cholesterol, rejection episodes, infection episodes, surgical mortality, and development of malignancy were examined. Induction immunosuppression was used in all patients after primary transplantation. A prospective PRA screen was performed in all patients. A PRA in excess of 10% required a negative donor-specific lymphocyte crossmatch before transplantation. In addition to routine light microscopy, immunofluorescence staining of endomyocardial biopsy specimens was performed in the majority of patients (n = 268). Rejection was characterized as cellular, vascular (humoral), or mixed according to previously described criteria [3, 4]. Surveillance biopsies and coronary angiograms were performed as per protocol.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Karwande, Division of Cardiothoracic Surgery, University of Utah Medical Center, 50 North Medical Dr, Salt Lake City, UT 84132.

© 1992 by The Society of Thoracic Surgeons

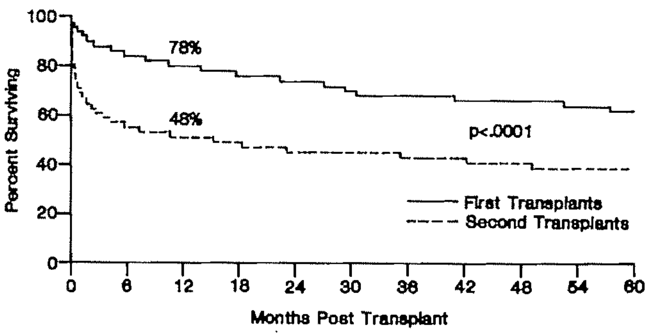


Fig 1. (ISHLT registry data.) Actuarial analysis of survival of second transplant recipients and a matched group of first transplant recipients demonstrating a decreased survival (78% versus 48%) in the retransplantation group.

Statistics

Univariate analysis of the relationship between risk factors and survival was performed by Tarone-Ware analysis of the actuarial survival curves. Multivariate analysis of actuarial survival was performed using a logistic stepwise regression model. Differences between groups were analyzed using χ^2 tests or Fisher's exact test for discrete variables and t tests for continuous variables. Values are reported as mean ± standard error of the mean. A p value of less than 0.05 was considered statistically significant.

Results

ISHLT Registry Data

Accelerated allograft coronary artery disease was the cause of graft failure in 63% of recipients. Rejection and nonspecific graft failure contributed 18% and 19%, respectively.

The 1-year actuarial survival for second transplants was significantly lower: 48% compared with 78% for first transplants ($p < 0.001$). This was principally due to a high early mortality of 15% in retransplants (Fig 1). Beyond 6 months patients in both groups did not exhibit significant differences in long-term survival (Fig 2).

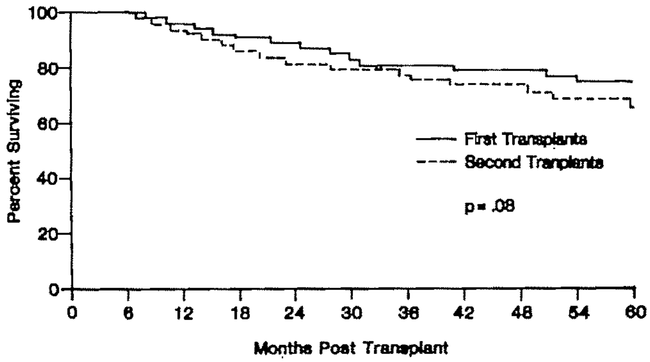


Fig 2. (ISHLT registry data.) Actuarial analysis of survival of patients surviving greater than 6 months after either repeat or primary cardiac transplantation, demonstrating no significant difference in the long-term survival between the two groups.

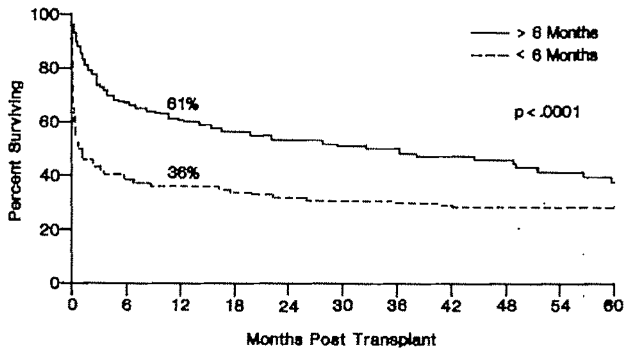


Fig 3. (ISHLT registry data.) Actuarial analysis of survival of patients with intervals between transplantations of greater than and less than 6 months demonstrating a significant difference (greater 61% 1-year survival in patients with a shorter interval).

Recipient sex and age did not affect survival after repeat transplantation. Survival was greater in patients undergoing retransplantation after 1985 (1 year survival, 52%) compared with those undergoing transplantation before 1985. In terms of immunosuppressive regimens, patients who were treated with triple-therapy regimens (azathioprine, cyclosporine, and steroids) after retransplantation fared better than those on other protocols.

The interval between transplantations was a significant predictor of survival. Patients with an interval of greater than 6 months between the first and second transplantation had significantly greater survival than those undergoing retransplantation within 6 months (1 year survival, 61% versus 36%; $p < 0.001$) (Fig 3). Patients having retransplantation for ACAD had significantly longer intervals between transplants compared with patients receiving transplants for rejection. Mechanical assistance preoperatively was required more often in patients undergoing retransplantation for rejection or nonspecific graft failure when compared with patients having transplantation for ACAD (80% and 86% versus 36%; $p < 0.005$). Patients requiring mechanical support and those having retransplantation for intractable rejection both had lower survival rates (Fig 4). Experience of the transplant center did not affect survival in repeat transplant recipients. One-year survival was 40% for centers having performed less than 30 transplantations at the time of the index repeat transplantation as compared with 50% for centers with greater than 30 transplantations performed (p = not significant).

Multivariate stepwise logistic regression analysis identified interval between transplantations, cause of allograft failure, and year of transplantation as the most important predictive variables. An "ideal candidate" was defined as a retransplant patient with allograft failure due to an interval between transplantations of greater than 6 months, with a date of second transplantation after 1985, and without preoperative mechanical support. Patients meeting these criteria had a 1-year survival of 64%, still lower than the survival rate of 79% for first transplant recipients.

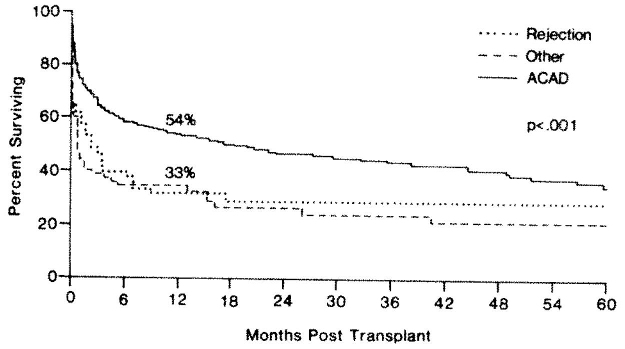


Fig 4. Actuarial survival of patients reported to the ISHLT registry after repeat transplantation for either accelerated allograft coronary artery disease (ACAD), rejection, or nonspecific graft failure. Rejection and nonspecific graft failure patients had a significantly decreased survival.

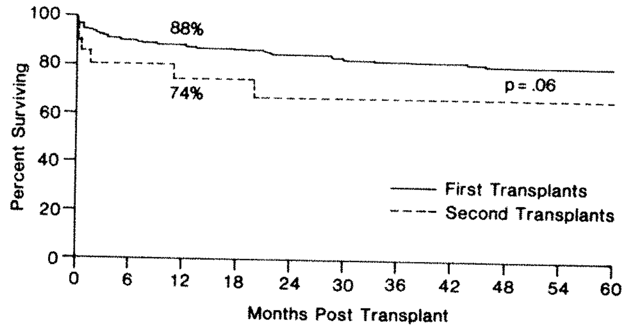


Fig 5. Actuarial analysis of survival in patients with second transplants reported in the Utah Cardiac series. Survival after repeat transplantation was greater in the Utah series than that observed in the registry patients.

Utah Cardiac Data

Characteristics of patients undergoing repeat transplantation with the Utah group are similar to the ISHLT group with respect to age and sex. Accelerated allograft coronary artery disease was the cause of graft failure in 50% of the patients. Rejection and nonspecific graft failure contributed 40% and 10%, respectively (Table 1). Compared with the ISHLT data, a greater proportion of patients in the Utah group underwent retransplantation for acute rejection as the cause of allograft failure (40% versus 18%; $p = 0.03$). Despite the greater proportion of patients having retransplantation for acute rejection, the Utah series had a higher 1-year survival compared with the ISHLT group (1-year survival, 74% versus 48%) (Fig 5). In the Utah series the initial hospital mortality (30 days) was 15% in the retransplant group compared with 2.5% in the primary transplant group ($p = 0.43$). No difference in long-term survival was observed between patients surviving greater than 6 months after either primary or repeat transplantation (Table 2).

Patients undergoing retransplantation within 6 months of the primary transplant showed a trend toward decreased survival (1-year survival, 56% versus 91%; $p = 0.24$). All patients receiving transplants within 6 months of the primary transplantation had rejection or a nonspecific cause for allograft failure. Patients undergoing retransplantation for ACAD had significantly longer intervals between transplantations (26.4 months versus 4.2 months; $p < 0.001$).

The incidence of surgical complications was markedly increased in the retransplantation group. The operating room mortality was 10% compared with 1.5% in the primary transplant recipients ($p = 0.05$). The incidence of mediastinitis was also increased (10% versus 2.5%; $p = 0.11$). No difference was noted between first and second transplant recipients for the number of days to the first treated rejection episode (63 days versus 46 days; p = not significant) or number of rejection episodes in the first 4 months (1.3 versus 1.6; p = not significant). There was also no difference in the number of major infections during the first 12 months (0.56 versus 0.78; p = not significant).

Table 1. Characteristics of Patients Undergoing Retransplantation in the ISHLT Registry and Utah Cardiac Transplant Program

Variable	ISHLT Registry	Utah Cardiac
First transplant	421	420
Second transplant	449	20
No. of patients		
Age (y)	41.5 ± 0.7	48.8
Cause of allograft failure		
ACAD	63%	50%
Rejection	18%	40%
Nonspecific	19%	10%
Sex		
Male	80%	90%
Female	20%	10%
Mechanical assistance[a]		
First transplant	7%	10%
Second transplant	48%	20%

[a] Intraaortic balloon pump or ventricular assist device.

ACAD = accelerated allograft coronary artery disease; ISHLT = International Society for Heart and Lung Transplantation.

Table 2. Survival Characteristics of Patients in the Utah Cardiac Program Undergoing Repeat Transplantation

Variable	One-Year Survival	p Value
Patients surviving >6 months		NS
First transplants	98%	
Repeat transplants	92%	
Transplant interval		NS
>6 months	91%	
<6 months	56%	
Repeat transplantation		NS
For ACAD	90%	
For Rejection	56%	

ACAD = accelerated allograft coronary artery disease.

Table 3. HLA Sensitization in Primary and Repeat Transplants in the Utah Cardiac Transplant Program

Variable	First Transplant	Second Transplant
PRA >10%	2.7%	20%
Positive crossmatch	2.8%	15%

PRA = Panel reactive antibody.

HLA matching data with regard to the second donor were available in 15 of 20 patients. In 13 patients (87%) there was repetition in the second donor heart of mismatched HLA antigens in the first allograft. The 1-year survival in this group with repeated mismatched antigens was 77%. Patients undergoing retransplantation exhibited a greater degree of sensitization as evidenced by a higher mean PRA and a 15% incidence of positive retrospective donor-specific lymphocyte crossmatch compared with 2.8% in primary transplant recipients ($p = 0.02$) (Table 3). Two of 3 patients with a positive crossmatch died.

Based on immunofluorescence of endomyocardial biopsy specimens all transplant patients were classified as manifesting predominantly vascular, mixed, or cellular rejection. Patients classified as having a vascular pattern of rejection had a distinctly poorer survival. The risk of development of allograft coronary disease was higher in patients with vascular or mixed rejection pattern. Angiographically determined incidence of coronary artery disease was 15% (63/420). Of these 63 patients, 51 patients (80%) had either a vascular or mixed biopsy pattern. Immunofluorescence biopsy data were available for both the first and second transplants on 11 recipients. All except 1 patient repeated their biopsy pattern in the second transplant.

In comparing patients requiring retransplantation for ACAD with other patients requiring retransplantation no differences were found in serum cholesterol levels or age of donor hearts. Serum cholesterol levels were significantly ($p < 0.02$) higher in patients receiving corticosteroids. Patients who were listed as UNOS status 1 before retransplantation had a lower survival (1-year survival, 60% versus 90%; p = not significant). The requirement of mechanical assistance (intraaortic balloon pump or ventricular assist device) was doubled in the retransplant group in comparison with primary transplants (20% versus 10%; p = not significant) (see Table 1).

Although the incidence of rejection and infection did not differ between the first and second transplant recipients, the incidence of malignancy was increased after repeat transplantation (5% versus 2.3%; $p = 0.39$).

Comment

Only a few centers have reported their experience with retransplantation [5–7]. To review a broad spectrum of patients we decided to analyze the ISHLT data and our own. Several of the questions that clinicians are faced with when making decisions regarding the candidacy of a patient for retransplantation were considered.

Survival

In the ISHLT registry data two closely matched patient groups were compared. The survival in the retransplant group was markedly decreased (1-year survival, 48% versus 79%; $p < 0.001$) compared with that in primary transplant recipients, with the majority of the increased mortality occurring in the early posttransplantation period. Although a trend toward decreased survival in retransplantation patients was also observed in the Utah group (1-year survival, 74% versus 88%; $p = 0.06$), this difference was less marked than in the ISHLT data. Most individual centers [5, 7] and ISHLT have reported markedly decreased survival in retransplantation patients. In the Columbia series [6], survival was no different. Here we report a trend toward slightly decreased survival that did not achieve statistical significance. Recipients of second transplants in the Utah Cardiac series had greater survival than those in the ISHLT registry despite a higher percentage of patients undergoing retransplantation for intractable rejection in the Utah Cardiac series (see Fig 5). In both groups patients surviving beyond 6 months after repeat transplantation had a long-term survival not significantly different than that in patients surviving 6 months after primary transplantation. The ISHLT registry patients having retransplantation due to rejection as the cause of allograft failure had a decreased survival (1-year survival, 33%) when compared with those receiving transplants for ACAD (see Table 2). A similar trend was also seen in the Utah series (1-year survival, 56% versus 90%; $p = 0.25$) but did not achieve statistical significance because of the small numbers. The shorter interval between transplantations and greater hemodynamic instability observed may be the main factors contributing to the decreased survival seen in patients undergoing transplantation for rejection [5, 8].

Mechanical Assistance

In both the ISHLT registry (48% versus 7%) and Utah Cardiac (20% versus 10%) series retransplant patients were more likely to require mechanical assistance. In both series patients having retransplantation for nonspecific graft failure or rejection were more likely to require mechanical support than those having retransplantation for ACAD.

Transplantation Interval

In the ISHLT registry there was a marked impact on survival between patients receiving transplants within 6 months of the first transplantation as compared with those receiving transplants with an interval of greater than 6 months (1-year survival, 36% versus 61%; $p < 0.001$) (see Fig 3). A similar trend was observed in the Utah Cardiac series, although the difference (1-year survival, 56% versus 91%) did not approach statistical significance ($p = 0.24$) (see Table 2). In the Utah series all patients undergoing transplantation within 6 months of the primary transplantation had either rejection or a nonspecific cause for allograft failure. Several factors may be responsible for the improved survival in recipients with a longer interval between first and second transplantations. Because immunosuppressive requirements are higher initially, those with a longer interval between transplantations are likely to be receiving lower doses of immunosuppressive agents and corticosteroids at the time of repeat transplantation. Additionally they have had time to recover from the first transplant operation.

In the Utah group, trends toward decreased survival were observed in retransplant patients with shorter intervals between transplantations and in those with rejection as the cause of allograft failure, but these differences did not achieve statistical significance. The failure of these differences to achieve statistical significance may in part be due to the smaller number of patients in the Utah series.

Infection, Rejection, and Malignancy

Prolonged high-level immunosuppression during retransplantation may predispose the recipient toward infection or malignancy. Analysis of the data from the Utah Cardiac series confirms the observation made by others [5, 6] that rejection and infection episodes do not occur more frequently in recipients of second allografts. In the Utah Cardiac series patients undergoing repeat transplantation had an incidence of malignancy of 5% compared with 2.3% in primary transplant recipients ($p = 0.39$). Rejection pattern as defined by immunofluorescence microscopy (vascular, mixed, or cellular) was repeated from the first to the second transplantation in all but 1 patient. Patients with a vascular rejection pattern tend to have lower survival. An increased incidence of allograft coronary artery disease is seen in patients who manifest vascular and mixed rejection patterns in biopsy specimens [9]. It is conceivable that in the future this might become one of the factors to be considered when deciding on the candidacy of a retransplant patient.

Surgical Complications

Retransplant recipients both in the ISHLT registry and the Utah cardiac series exhibited an increased mortality in the early posttransplantation period. In the Utah series these patients had a higher incidence of mediastinitis, probably related to their hemodynamically unstable status and greater level of immunosuppression.

Antigenic Status

Recipients undergoing repeat transplantation had a much higher incidence of sensitization to the standard panel of antigens than candidates for primary transplantation (see Table 3). Blood transfusions and exposure to donor-specific antigens of the first allograft may contribute to increased sensitization. In the Utah series, 13 retransplanted patients had repetition in the second allograft of HLA antigens present in the first allograft. This did not affect survival (1-year survival, 77%), as has been reported in renal transplantation [10, 11]. The clinical implication of this observation is that preoperative donor HLA typing and crossmatching is probably indicated only in recipients who are highly sensitized as shown by a high panel reactive antibody titer.

Conclusions

Survival is decreased in patients undergoing repeat transplantation compared with patients undergoing primary transplantation. Patients having retransplantation for rejection and within 6 months of the first transplantation tend to have lower survival rates. Operative mortality (24 hours) and hospital mortality (30 days) are markedly increased after repeat transplantation. The requirement of preoperative mechanical assistance is high in second transplant recipients, especially those having retransplantation for rejection and nonspecific graft failure. Most patients undergoing retransplantation for rejection and nonspecific graft failure require retransplantation within 6 months of the primary transplantation. Most patients having retransplantation for ACAD do not require retransplantation until 6 months or longer after the primary transplantation. Infection and rejection do not occur more frequently after repeat transplantation. If the early mortality can be overcome, the long-term survival is excellent. Immunofluorescence of myocardial biopsy specimens could be helpful as a predictor of accelerated graft atherosclerosis. In deciding the candidacy of a recipient for repeat transplantation the above factors should be considered.

References

1. Kriett JM, Kaye MP. The Registry of the International Society for Heart and Lung Transplantation: eighth official report—1991. J Heart Lung Transplant 1991;10:491–8.
2. Kriett JM, Kaye MP. The Registry of the International Society of Heart Transplantation: seventh official report—1990. J Heart Transplant 1990;9:323–30.
3. Hammond EM, Ensley RD, Yowell RL, et al. Vascular rejection of human cardiac allografts and the role of humoral immunity in chronic allograft rejection. Transplant Proc 1991;23:26–30.
4. Hammond ME, Wittwer CT, Greenwood J, et al. Relationship of OKT3 sensitization and vascular rejection in cardiac transplant patients receiving OKT3 rejection prophylaxis. Transplantation 1990;50:776–82.
5. Dein JR, Oyer PE, Stinson EB, Starnes VA, Shumway NE. Cardiac retransplantation in the cyclosporine era. Ann Thorac Surg 1989;48:350–5.
6. Michler RE, McLaughlin MJ, Barr ML, et al. Clinical experience with cardiac retransplantation. J Thorac Cardiovas Surg (in press).
7. Cabrol C, Gandjbakhch I, Pavie A, et al. Is the use of artificial hearts the future solution for interim treatment of patients awaiting retransplantation? Transplant Proc 1989;21:3658–9.
8. DeBoer J, Cohen B, Thorogood J, Zantvoort FA, D'Amaro J, Persijn G. Results of acute heart retransplantation. Lancet 1991;337:1158.
9. Hammond EM, Yowell RL, Price GL, et al. Vascular rejection and its relationship to allograft coronary artery disease. J Heart Lung Transplant 1992;11:111–9.
10. Stratta RJ, Choong-San O, Sollinger HW, Pirsch JD, Kalayoglu M, Belzer FO. Kidney retransplantation in the cyclosporine era. Transplantation 1988;45:40–5.
11. Almond PS, Matas AJ, Gillingham K, et al. Risk factors for second renal allografts immunosuppressed with cyclosporine. Transplantation 1991;52:253–8.

DISCUSSION

DR ADNAN COBANOGLU (Portland, OR): I congratulate the Utah team for their outstanding results in a very difficult group of transplant patients and also for their contributions in heart transplantation over the years. We have a much more sobering experience in Oregon at the University Hospital in Portland. Since December 1985 we have performed 175 heart transplantations and 9 of them were second transplantations; only 3 patients survived up to 1 year. So the 1-year survival is in the mid-30% range, and those who survived underwent transplantation early and for rejection. This is within weeks to months of the first transplantation. So these patients are extremely difficult to deal with. Your results are quite good, although not as good as the first-time transplantations.

We have found ourselves at times having to deal with your last conclusion, the philosophical dilemma, as to whether we should allocate a second or a third heart to those patients who may need them.

I have felt that the reason the 3 patients in whom we performed retransplantation survived was because they had not been on chronic immunosuppression and chronic steroid therapy in terms of many months or years. Now, we know, and the literature is replete with reports, that any major operation carries a high risk if patients have been on chronic steroid therapy, for whatever reason. I would have expected these patients to have a relatively higher risk overall of wound complications and mediastinitis, much more than your slides showed, and that actually may be the experience in other active centers in the country.

In any case, I congratulate you for your results and let you know of this sobering note from your northern neighbor state.

DR PETER P. McKEOWN (Tampa, FL): I also compliment Dr Karwande and associates and would like to ask them if they could fill a gap in our knowledge. We also have been somewhat concerned about vascular rejection and its role for retransplantation or recurrent rejection. Have you looked at the incidence or the frequency of cytotoxic antibodies in your patient cohort, and has that seemed to be related to immunosuppression, that is, is it more frequent in patients treated with OKT3 versus the non-OKT3 induction group?

Second, I compliment you on using the immunoperoxidase. If you did have positive immunoperoxidase in a patient who was going to be a retransplantation candidate, would you again alter your immunosuppression and perhaps have a broader spectrum with MALG or RATG?

DR KARWANDE: Let me start first with Dr Cobanoglu. We were also surprised with the low level of infection in these patients. I think the possible explanation for that would be that infection is related to the level of immunosuppression at the time of retransplantation. On the other hand, the incidence of malignancy, which we also looked at but I did not allude to in this presentation, is probably more representative of the cumulative level of immunosuppression.

In terms of the level of sensitization, we have a protocol for patients on OKT3 management in which we monitor plasma levels of OKT3 as well as CD3 lymphocytes. We are extremely aware of xenosensitization when patients have required prolonged therapy with OKT3. In terms of immunosuppression, most of our patients had induction immunosuppression for the first transplant, and for the second transplant standard triple-therapy immunosuppression was used.

Specifically, in response to Dr McKeown's question regarding cytotoxic antibodies, we obtain a PRA level before transplantation. In the last 6 months we have started monitoring donor-specific antibodies at regular intervals. Patients undergoing retransplantation with vascular rejection and immunofluorescent positivity will require more aggressive immunosuppression.

Acute Rejection of Lung Allografts With Various Immunosuppressive Protocols

Bartley P. Griffith, MD, Robert L. Hardesty, MD, John M. Armitage, MD,
Robert L. Kormos, MD, Gary C. Marrone, MD, Steve Duncan, MD, Irvin Paradis, MD,
James H. Dauber, MD, Samuel A. Yousem, MD, and Penny Williams, MD

Department of Surgery, Division of Pulmonary Medicine, Department of Pathology, and Division of Infectious Disease, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Between February 1990 and December 1991, 69 patients who survived for a minimum of 5 days after single-lung (27), double-lung (32), or heart-lung transplantation (10) were studied to learn the incidence and severity of acute rejection and the possible effects of various immunosuppressive protocols on this rejection. Acute rejection was less common (2.1 versus 3.1 episodes/patient) after transplantation in those 30 candidates who received rabbit antithymocyte globulin for the first 5 postoperative days versus the 28 who were maintained on cyclosporine, azathioprine, and prednisone alone ($p < 0.05$), but no patient escaped at least one episode. Patients given cyclosporine received more 3-day courses of methylprednisolone ($p < 0.02$) than those given rabbit antithymocyte globulin (2.5 versus 1.7 courses). Although no disadvantage in terms of infectious morbidity was noted in the rabbit antithymocyte globulin group, no obvious intermediate advantage was noted in survival (85% at 12 months) or grade of rejection or airway flows. The most common histopathologic grades were mild (A2) and moderate (A3); the average grade was A2.3. FK 506 was tested in 11 patients, and early results are promising relative to low early and likely fewer late episodes of rejection. No differences were noted in the likelihood of rejection for any procedures.

(Ann Thorac Surg 1992;54:846–51)

Pulmonary transplantation has become increasingly accepted as therapy for select patients with end-stage diseases of the lung's parenchyma and blood vessels. Although a uniform grading of rejection proposed by the Lung Rejection Study Group of the International Society of Heart and Lung Transplantation [1] has detailed the histology associated with the allogenic response, little attention has been focused on the incidence, severity, and immunosuppressive modifiers of acute pulmonary rejection. From our entire experience of 193 various pulmonary transplant procedures since 1982, we have studied 69 patients who have survived operations between February 1990 and December 1991. Review of the recent experience permits comparison of the type of transplant and current immunosuppressive protocols, including cyclosporine (CsA), prednisone, and azathioprine with and without an adjuvant cytolytic and a newly introduced FK 506 regimen.

Material and Methods

Between February 1990 and December 1991, 69 patients survived at least 5 days after transplantation. A minimal 5-day survival was required so that varied immunosuppressive protocols were maintained and assessment of acute rejection assured. Twenty-seven patients received single lungs and 32 and 10 were treated with double-lung and heart-lung transplantation, respectively. Pulmonary hypertension from congenital heart disease (15) or primary pulmonary hypertension (13) was the most common indication for transplantation. Chronic obstructive lung disease was diagnosed in 19 patients, including 8 with α_1-antitrypsin deficiency. Thirteen patients had septic lung disease from cystic fibrosis (11), and other conditions included idiopathic pulmonary fibrosis (4), sarcoid (3), lymphangiomyomatosis (1), Kartagener's syndrome (1), immotile cilia syndrome (1), and graft versus host disease (1) (Table 1). Disease-specific indications for the various forms of transplantation included our belief that both lungs should be removed for septic lung diseases and that heart-lung transplantation is performed for complicated Eisenmenger syndrome and when right or left heart function is significantly abnormal (ejection fraction of the right and left ventricle <0.15 and <0.35, respectively).

Cyclosporine, azathioprine, and prednisone provided the maintenance immunosuppression for all but 11 patients in whom FK 506 was substituted for CsA. Between February 1990 and April 1991, all 26 surviving patients received rabbit antithymocyte globulin (RATG), 2 mg $\cdot$ kg^{-1} $\cdot$ day^{-1} for the first 5 postoperative days (RATG group). This serum was produced in our surgical research laboratory. To avoid the need for CsA immediately postoperatively, 4 additional patients between July 1991 and December 1991, who were in hemodynamically unstable condition, were given RATG. These recipients were compared with 28 others operated on between May 1991 and December 1991 who did not receive RATG (CsA group).

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Griffith, Department of Surgery, University of Pittsburgh School of Medicine, 1084 Scaife Hall, Pittsburgh, PA 15261.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

The age, sex, and HLA mismatches were similar between RATG and CsA groups, as were CsA and prednisone doses (Table 2). The average dose of azathioprine was higher in the CsA group at 1.4 mg · kg^{-1} · day^{-1} versus 0.8 mg · kg^{-1} · day^{-1} in the RATG group ($p < 0.01$). The latter patients were followed up for a mean of 334 days compared with the CsA patients, who had more recent transplantation (161 days). More single-lung and no heart-lung procedures were performed in the CsA patients. The allograft ischemic times were similar at 271 minutes (range, 90 to 435 minutes) and 313 minutes (range, 180 to 435 minutes) for RATG and CsA, respectively.

Of the 11 patients who were treated with FK 506 as a substitute for CsA, 3 were randomly selected adults, and the remainder were successive children who underwent transplantation between August 1991 and December 1991. The FK 506 patients' ages averaged 18 years (range, 6 to 36 years), and only 3 were female. Immunosuppressive doses averaged 0.4 mg/kg for FK 506, 1.4 mg/kg for azathioprine, and 0.3 mg/kg for prednisone.

Acute rejection was diagnosed when transbronchial biopsy was graded between A1 and A4 based on the Lung Rejection Study Group [1] or when a sudden diffuse opacification was noted on the chest radiograph that was determined by bronchoalveolar lavage not due to infection. Confirmation of rejection required resolution of the radiographic abnormality after treatment or by transbronchial biopsy performed within 24 to 36 hours of treatment. Adults received 3 daily doses of 1 g of methylprednisolone. In the children, the doses were individually prescribed at 15 mg/kg for 3 days. Treatment generally followed a histologic grade of A2 or greater unless the clinical situation (infection) dictated otherwise. Transbronchial biopsies were performed every 2 weeks for 6 weeks and every 4 to 6 weeks for 3 months. Thereafter, surveillance transbronchial biopsies were completed every 3 months unless clinically indicated by a sustained fall in forced expiratory volumes and forced expiratory flows.

Pulmonary infections were often suspected clinically by radiograph, fever, and leukocytosis, but diagnosis was confirmed by bronchoalveolar lavage cultures. Preoperative antibiotics included ceftazidime and clindamycin and were continued for 5 days unless cultures from donor airways at implantation suggested alternative therapy. All patients with septic lung disease received prophylactic coverage based on preoperative culture and sensitivities. Prophylaxis for cytomegalovirus was given for all except those seronegative recipients of seronegative lungs. Three different 90-day protocols were followed, including oral acyclovir (<2,400 mg/day), intravenous ganciclovir, 5 mg/kg (adjusted for creatinine level > 123.8 μmol/L [1.4 mg/dL]), and ganciclovir for 6 weeks followed by oral acyclovir (3,200 mg/day) for a total of 3 months.

Table 1. Disease-Specific Indication for Various Forms of Pulmonary Transplantation

Indication	Single-Lung	Double-Lung	Heart-Lung	Total
Primary pulmonary hypertension	4	7	2	13
Congenital heart disease	1	8	6	15
Chronic obstructive lung disease	14	3	2	19
Cystic fibrosis		11		11
Immotile cilia syndrome		1		1
Kartagener's syndrome		1		1
Sarcoid	3			3
Idiopathic pulmonary fibrosis	4			4
Graft versus host disease		1		1
Lymphangiomyomatosis	1			1
Total	27	32	10	69

Table 2. Acute Rejection[a]

	Immunosuppression		
Variable	RATG, CsA, Pred, AZA	CsA, Pred, AZA	Total or Average
No. of Patients	30	28	58
Age (y)	39 (14–56)[b]	40 (11–60)	39 (11–60)
M/F	14/16	14/14	28/30
Postop days	334	161	248
Dose (mg · kg^{-1} · day^{-1})			
CsA	9.7	7.8	8.8
Pred	0.2	0.2	0.2
AZA	0.8	1.4	1.0
Transplantation			
Single-lung	9	17	26
Double-lung	14	11	25
Heart-lung	7	0	7

[a] HLA A,B,Dr mismatches were not different between groups ($p >$ 0.05). [b] Numbers in parentheses are ranges.

AZA = azathioprine; CsA = cyclosporine; Pred = prednisone; RATG = rabbit antithymocyte globulin.

Patient survival and freedom from acute rejection was calculated by life-table analysis, and differences in RATG and CsA groups were determined by Mantel-Cox and Breslow analyses. Rejection grades A1 through A4 were averaged for the entire period of follow-up and also for postoperative time intervals of less than 30, 30 to 90, and more than 90 days. Two-tailed t testing was used to determine differences in grades of rejection. The FK 506 patients were judged too few and too different in age to be fairly compared with the CsA and RATG groups.

Results

Six-month and 12-month survivals were similar in the groups (Fig 1). Eighty-two percent of RATG patients and 89% of the CsA group had cumulative probabilities of being alive 1 year after pulmonary transplantation. Four of 30 RATG patients died of rejection (1), infection/preservation injury (2), pancreatitis (1), and intracerebral bleed (1). Three of 28 CsA patients died of infection (2) and infection/preservation injury (1).

Rejection was common in both groups as all CsA patients and 70% of RATG patients had at least one episode within 6 months of transplantation (Fig 2). This difference was significant ($p < 0.005$), but in time all

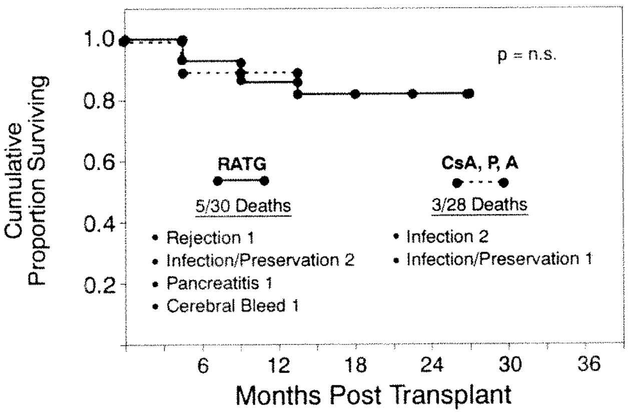


Fig 1. Operative survivors. (A = *azathioprine;* CsA = *cyclosporine;* n.s. = *not significant;* P = *prednisone;* RATG = *rabbit antithymocyte globulin.*)

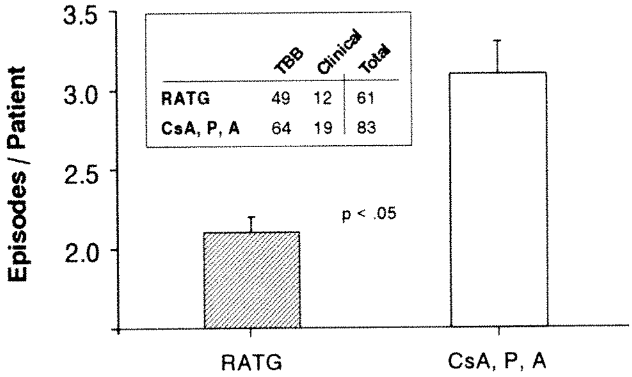


Fig 3. Incidence of pulmonary rejection. (A = *azathioprine;* CsA = *cyclosporine;* P = *prednisone;* RATG = *rabbit antithymocyte globulin;* TBB = *transbronchial biopsy.*)

RATG patients had evidence of acute rejection by transbronchial biopsy. In spite of the longer follow-up, RATG patients had significantly fewer ($p < 0.05$) episodes (2.1) of rejection than CsA recipients (3.1) (Fig 3). Accordingly, CsA patients required a greater number of 3-day courses of methylprednisolone (Solu-Medrol; Upjohn Co, Kalamazoo, MI) (2.5 versus 1.6; $p < 0.02$). Twelve of 61 and 19 of 83 episodes for RATG and CsA patients, respectively, were initially diagnosed from sudden opacification of the chest radiograph. When the episodes were divided by postoperative interval, more occurred in the first 30 days, and the CsA group had a significantly higher average number at less than 30 days ($p < 0.005$) and 30 to 90 days ($p < 0.05$) but not at more than 90 days (Fig 4). The average grade of histologic rejection varied narrowly between groups (2.2 to 2.5) and also was not significantly different at any time interval (Table 3). The overall distribution of histologic rejection shows that more biopsy specimens were graded as A1 in the RATG group and more were A2 in the CsA group (Fig 5). The distribution of histologic grade of rejection shows that A2 was most common in CsA patients at less than 30 days but was noted equally with A3 thereafter (Fig 6). Grade A3 rejection was more common than grade A2 in RATG patients at less than 30 days, but the opposite was true between 30 and 90 days (Fig 7). The RATG group averaged significantly more days to the first and second episodes at 32 versus 16 days ($p < 0.04$) and 66 versus 34 days ($p < 0.05$). When acute rejection was compared with the type of procedure performed, no difference was noted at any time interval (Table 4).

The incidence of infection was similar in both groups (Table 5). Infections usually began in the lungs and were responsible for five of seven deaths. Bacterial pneumonia was most frequent in the first 30 days and was diagnosed as early as 2 days and as late as 46 days. *Staphylococcus aureus* (2), *Pseudomonas aeruginosa* (5), *Enterobacter* (2), and *Acinetobacter* (3) predominated. Fungal pneumonia was caused by *Aspergillus* species and occurred in the setting of prolonged broad-spectrum antibiotic in 1 and was thought to arise in the remaining host diseased lung in

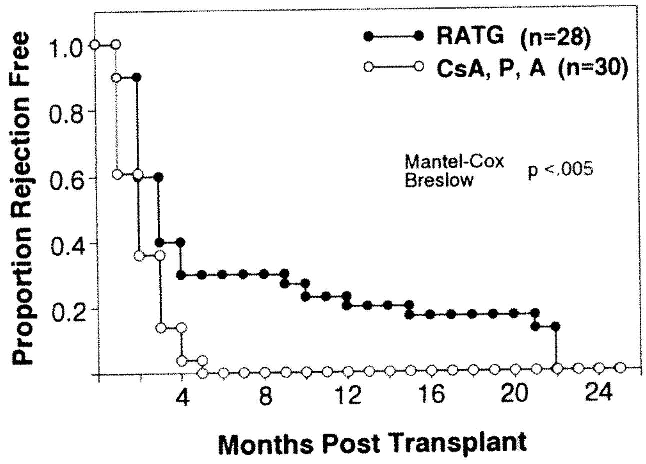


Fig 2. Proportion of patients free of rejection. (A = *azathioprine;* CsA = *cyclosporine;* P = *prednisone;* RATG = *rabbit antithymocyte globulin.*)

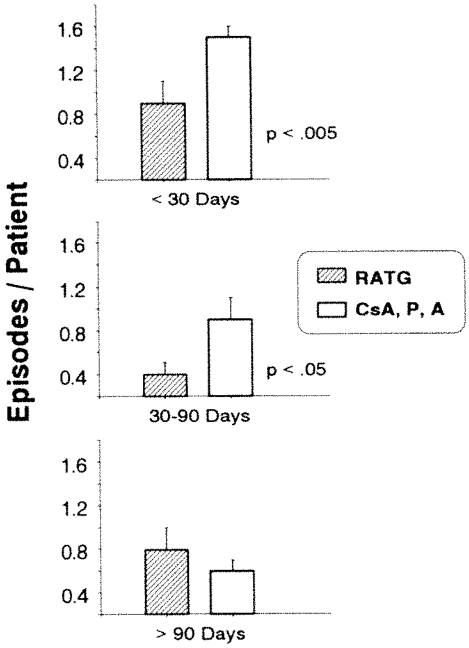


Fig 4. Postoperative interval to rejection. (A = *azathioprine;* CsA = *cyclosporine;* P = *prednisone;* RATG = *rabbit antithymocyte globulin.*)

Table 3. Histologic Rejection—Average Grade[a]

Postop Days	RATG	CsA, Pred, AZA
<30	2.3 (19)	2.3 (30)
30 to 90	2.2 (12)	2.5 (21)
>90	2.4 (13)	2.4 (12)

[a] Numbers in parentheses are numbers of episodes.

AZA = azathioprine; CsA = cyclosporine; Pred = prednisone; RATG = rabbit antithymocyte globulin.

another who received a single lung transplant. Viral infections included primary and reactivation cytomegalovirus, donor-acquired herpes simplex virus, and post-transplantation lymphoproliferative disease. The latter overwhelmed single-lung allografts in 2 patients and required retransplantation that was successful.

Functional comparisons between groups was attempted by measurement of expiratory flows and volumes in those patients with double-lung and heart-lung implants. Recipients of single-lung transplants were too heterogeneous to include as the remaining lung was affected with various diseases, some of which markedly affected spirometric values. At 90 days no difference was noted in the forced expiratory volume in the RATG (2.33 L) or CsA group (2.13 L). The forced expiratory flow was also similar, with values of 2.9 and 2.1 L, respectively.

The FK 506 group, with 1.1 episodes per patient, seemed to follow the low incidence of rejection recorded in the RATG group (0.9 episodes/patient) early after transplantation (Fig 8). Later the rate of acute rejection was 0.2 episodes per patient. The mean grade of rejection at less than 30 days was A1.7. All FK 506 patients survived, but 1 patient died of *Aspergillus* infection after double-lung transplantation for cystic fibrosis. This recipient was mortally ill with terminal respiratory failure and sepsis before ill-advised transplantation.

Comment

This study of acute rejection after single-lung, double-lung, and heart-lung transplantation has shown that mild and moderate grades are common and should be anticipated. Unlike our cardiac recipients [2], lung transplant recipients virtually never escape an early episode and require frequent surveillance by transbronchial biopsy and examination of chest radiograph, arterial desaturation, and clinical signs, including fever, shortness of breath, and generalized fatigue. Although the frequency of reported rejection is related to the number and frequency of biopsies [3], we believe given the short-term and long-term adverse consequences of undiagnosed rejection, which include sudden dysfunction and obliterative bronchiolitis, that aggressive therapy is justified [4, 5].

Our retrospective review is limited by an imperfect comparison between those who received RATG and those who did not. However, the series are contemporary, and no real differences existed in the groups that would have obvious effects on the incidence, severity, and consequence of rejection. Traditionally, induction-cytolytic therapy has been used after lung transplantation, but it seemed reasonable to test the need because our experience in cardiac transplantation had not borne out justification for prophylactic therapy with either polyclonal RATG or the monoclonal OKT3. Our choice of RATG was

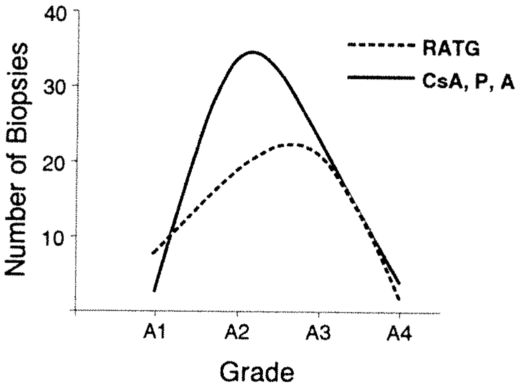


Fig 5. Distribution of histologic rejection. (A = azathioprine; CsA = cyclosporine; P = prednisone; RATG = rabbit antithymocyte globulin.)

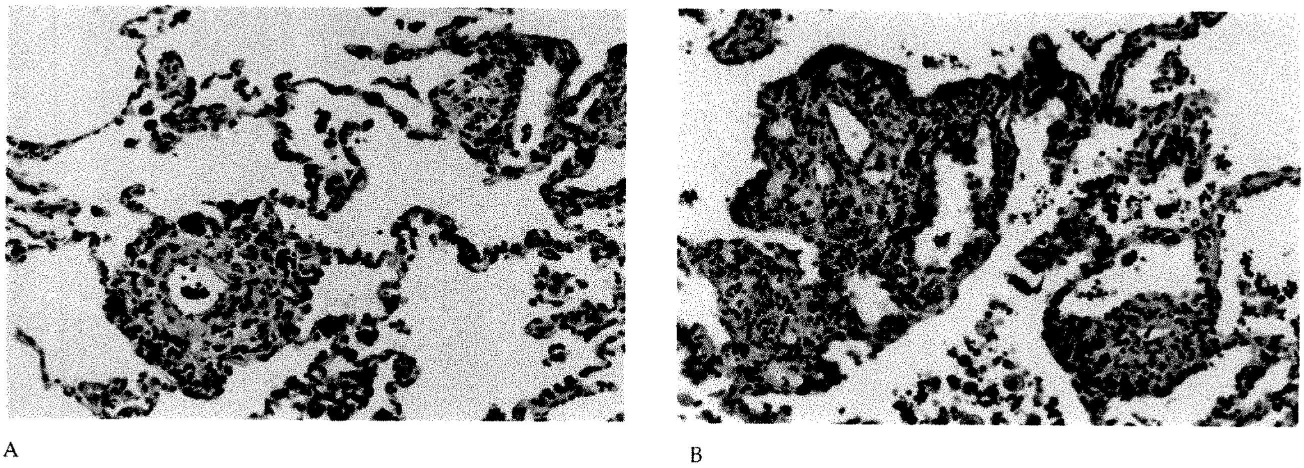


Fig 6. (A) Mild acute rejection (ISHLT grade A2). Lymphocytes are confined to perivascular interstitium and do not track into alveolar septa. (B) Moderate acute rejection (ISHLT grade A3). Perivascular lymphocytes cuff the small vessels of the lung and extend into alveolar septa. (Both ×64 before 50% reduction.)

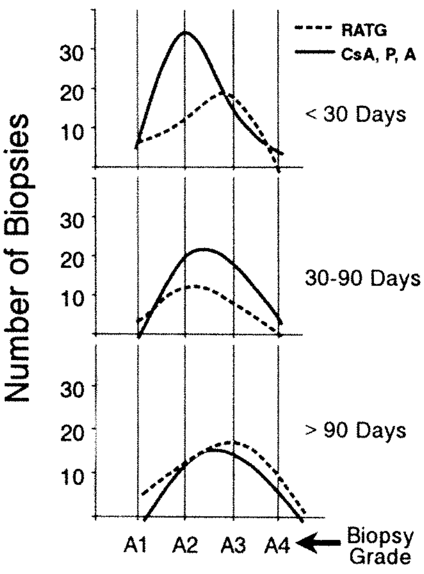


Fig 7. Distribution of rejection grade by postoperative interval. (A = azathioprine; CsA *= cyclosporine;* P *= prednisone;* RATG *= rabbit antithymocyte globulin.)*

based on our decade-long experience with this serum and our previous studies in cardiac recipients suggesting reduced acute rejection compared with OKT3 [2].

With the relatively high risk of pneumonia after lung transplantation compared with cardiac transplantation, we believed that less immunosuppression might reduce the incidence without significantly affecting the severity of rejection [6]. Before the advent of treatment protocols for cases of cytomegalovirus-seropositive donor organs or recipients, cytomegalovirus pneumonia was common and usually lethal [7]. To further lessen this risk and that of the potential linkage of cytomegalovirus and obliterative bronchiolitis [3], we hoped to avoid the routine use of RATG.

We and others [8] found that the overall risk of rejection is high, with most recipients afflicted within 30 days of operation. The impact of RATG was to reduce the early and mid-interval risk but not the late incidence, suggesting that no lasting effect was induced by the cytolytic therapy. Only 1 patient died of unrelenting acute rejection and obliterative bronchiolitis, but we know that this series is too young to demonstrate whether chronic rejection will be more common in either the CsA or RATG group [9]. To date at least, all survivors are out of the hospital and not requiring oxygen. No serious abnormalities or intergroup differences have been noted in airway flow rates measured at 90 days. The goal of limiting rejection seems reasonable as long as morbidity of cytolytic immunosuppression is not significant. We were surprised to find that the RATG group did not appear disadvantaged in this regard as the incidence of viral and bacterial infection was uniform and not overwhelming.

Table 4. Acute Rejection Episodes per Patient

Transplantation	<30 Days	30 to 90 Days	>90 Days
Single-lung	1.1	0.88	0.74
Double-lung	1.3	0.45	0.48
Heart-lung	1.2	0.36	0.72
Average	1.2	0.60	0.62

Table 5. Infection and Immunosuppression

Immuno-suppression	Bacterial Pneumonia	Fungal Pneumonia	CMV	HSV	PTLD
RATG (n = 30)	6	. . .	7[a]	4	3
CsA, Pred, AZA (n = 28)	8	2	8[b]	3	1

[a] Three primary, 4 secondary. [b] Three primary, 5 secondary.

AZA = azathioprine; CMV = cytomegalovirus; CsA = cyclosporine; HSV = herpes simplex virus; Pred = prednisone; PTLD = posttransplantation lymphoproliferative disease; RATG = rabbit antithymocyte globulin.

The experience with FK 506 as an immunosuppressant is evolving [10, 11], and its use in this study, primarily in children as a substitute for CsA, is encouraging. Early rejection appears similar to the RATG group, and late biopsies have been remarkable for few instances of acute alloreactive-related pathology. Certainly additional patients and more time are required to determine if FK 506 has a significant advantage.

In summary, although acute rejection is nearly universal early after pulmonary transplantation, it responds to prompt treatment with methylprednisolone but occasionally evolves to an unrelenting process. The common pathology of early rejection rests between mild grades in which blood vessel cuffing extends to interstitial spaces and moderate grades with the latter lymphocytes pushing through alveolar septae. Although RATG reduced early rejection episodes without an associated increase in infec-

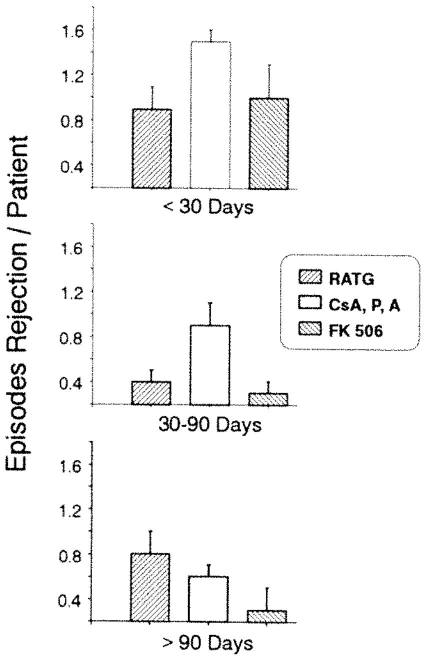


Fig 8. Postoperative interval to rejection for all three immunosuppression protocols. (A = azathioprine; CsA *= cyclosporine;* P *= prednisone;* RATG *= rabbit antithymocyte globulin.)*

tious morbidity, no apparent intermediate benefit in survival or function is obvious. FK 506 is potentially an important new drug as it may further reduce late rejection.

We give special thanks to Ann Lee, MSN, Sharon Armstrong, Diana Zaldonis, RN, BSN, Ko Bando, MD, and Joanne Gizzi for assistance with data and preparation of the manuscript.

References

1. Yousem SA, Berry GJ, Brunt EM, et al. A working formulation for the standardization of nomenclature in the diagnosis of heart and lung rejection. Lung Rejection Study Group. J Heart Transplant 1990;9:593–601.
2. Kormos RL, Armitage JM, Dummer JS, Miyamoto Y, Griffith BP, Hardesty RL. Optimal perioperative immunosuppression in cardiac transplantation using rabbit antithymocyte globulin. Transplantation 1990;49:306–11.
3. Scott JP, Fradet G, Smyth RL, et al. Prospective study of transbronchial biopsies in the management of heart-lung and single lung transplant patients. J Heart Lung Transplant 1991;10:626–37.
4. Scott JP, Higenbottam TW, Clelland CA, et al. Natural history of chronic rejection in heart-lung transplant recipients. J Heart Transplant 1990;9:510–5.
5. Glanville AR, Baldwin JC, Burke CM, Theodore J, Robin ED. Obliterative bronchiolitis after heart-lung transplant: apparent arrest by augmented immunosuppression. Ann Intern Med 1987;107:300–4.
6. Dummer JS, Montero CG, Griffith BP, Hardesty RL, Paradis IL, Ho M. Infections in heart-lung transplant recipients. Transplantation 1986;41:6:725–9.
7. Duncan AJ, Dummer JS, Paradis IL, et al. Cytomegalovirus infection and survival in lung transplant recipients. J Heart Lung Transplant 1991;10:638–46.
8. Clelland CA, Higenbottam TW, Stewart S, Scott JP, Wallwork J. The histological changes in transbronchial biopsy after treatment of acute lung rejection in heart-lung transplants. J Pathol 1990;161:105–12.
9. Griffith BP, Paradis IL, Zeevi A, et al. Immunologically mediated disease of the airways after pulmonary transplantation. Ann Surg 1988;208:371–8.
10. Todo S, Fund J, Demetris AJ, Jain A, Venkataramanan R, Starzl TE. Early trials with FK 506 as primary treatment in liver transplantation. Transplant Proc 1990;22:13–6.
11. Starzl TE, Fung J, Jordan M, et al. Kidney transplantation under FK 506. JAMA 1990;264:63–7.

DISCUSSION

DR R. MORTON BOLMAN III (Minneapolis, MN): This series is in keeping with the high quality of work we have come to identify with Dr Griffith and his group. You bring up a couple of very interesting points. First of all, we have struggled in our experience with the diagnosis of treatable rejection, much as we have gone back and forth over the years about heart transplant rejection. What do you do with a patient who has histological findings of rejection but has stable pulmonary function? This occurs primarily in the patient who is several weeks or more out from operation. Second, does the immunosuppressive regimen have an influence on obliterative bronchiolitis? In our lung and heart-lung recipients, who now total about 65 patients, we have about a 30% incidence of obliterative bronchiolitis in both groups. We have examined the influence of Minnesota ALG. About half of our patients have received it and half have not received it. We have not found any difference in the acute rejection incidence or in the incidence of obliterative bronchiolitis, and I would like to know if you have looked at your data in a similar manner.

DR GRIFFITH: I anticipated your question in terms of the obliterative bronchiolitis issue because it is the most pressing one, and obviously this type of comparison is going to be useful in time. I do not as yet have the data to properly address the issue because obliterative bronchiolitis is not a serious clinical problem, at least in our program, until at least a year or two.

With respect to trying to have a consistent trigger for the treatment of rejection, I do not know the appropriate trigger or threshold for treating histologic rejection. I will say that based on our fear that obliterative bronchiolitis is a form of chronic rejection that is difficult to cure, we tend to be aggressive with acute rejection of any histologic grade and treat it whenever possible with 1 g of Solu-Medrol daily for usually 3 days.

DR JOSEPH LADOWSKI (Fort Wayne, IN): Dr Griffith, I also would like to congratulate you on continuing to lead the way in this field, and also I would like to ask you a couple of questions. One is, how often do you see the case, as Dr Bolman mentioned, that you have histologic evidence without clinical evidence of rejection? Related to that question is the observation that the incidence of rejection is going to be related to how closely you look for it. Could you share with us your protocol for transbronchial biopsies?

DR GRIFFITH: We generally perform biopsy on a surveillance basis every 2 weeks for the first 6 weeks and then once a month for the next 3 months and thereafter about every 3 months, unless the clinical condition argues otherwise. We frequently see mild acute rejection grades in asymptomatic patients early after transplantation. Later these grades are less frequent and associated most often with obliterative bronchiolitis.

DR VAUGHN A. STARNES (Stanford, CA): Dr Griffith, I have listened to your presentation, and I really appreciate the work that has gone into that. One of the questions I must ask now is, what is your immunosuppressive regimen? You have given us good outcomes with three different ones. If we avoid steroids up front with our ATG protocol or maybe FK 506, do we get better bronchial healing than if we add steroids early on? Could you possibly allude to some of these dilemmas that we are, I guess, facing now that you have shown us three different protocols?

DR GRIFFITH: Our standing protocol is azathioprine and cyclosporine-based immunosuppression with 15 to 20 mg of prednisone begun at 14 days and tapered over 6 months if rejection is controlled. We do not believe the low doses of prednisone, even if started earlier, would cause a clinically significant decrease in bronchial healing. We will no longer use RATG as a routine because early survival is unchanged and we wish to compare FK 506 and cyclosporine without confounding adjuvants.

Improved Myocardial Ischemic Tolerance by Contractile Inhibition With 2,3-Butanedione Monoxime

James C. Stringham, MD, Karen L. Paulsen, BS, James H. Southard, PhD,
Barry L. Fields, MD, and Folkert O. Belzer, MD

Department of Surgery, University of Wisconsin Hospitals and Clinics, Madison, Wisconsin

Contracture of the arrested myocardium during prolonged storage of the heart results in both systolic and diastolic dysfunction, and is a major limitation to extended preservation. We studied the effects of a reversible contractile inhibitor, 2,3-butanedione monoxime (BDM), on myocardial ischemic tolerance. Isolated rabbit hearts were flushed with University of Wisconsin (UW) solution with and without 30 mmol/L BDM and 1 mmol/L CaCl, stored at 4°C for 24 hours, and subsequently reperfused for 60 minutes. Left ventricular pressure–volume relationships and adenine nucleotide content were determined before reperfusion. Left ventricular systolic pressure, diastolic volume, and adenine nucleotide content were measured after reperfusion. Hearts stored in UW solution underwent contracture and adenosine triphosphate (ATP) depletion during storage, and exhibited systolic dysfunction, impaired diastolic relaxation, and poor ATP regeneration upon reperfusion. The addition of calcium worsened contracture and ATP depletion ($p < 0.005$) and slightly improved function and ATP regeneration (p = not significant). Hearts stored in the presence of BDM experienced no contracture during storage; ATP was preserved (10.7 versus 15.7 nmol/mg; $p < 0.05$), and left ventricular systolic pressure and ATP content recovered to 74% and 93% of control on reperfusion, respectively ($p < 0.005$). Left ventricular diastolic volume remained depressed, however, although less than with UW solution (0.87 versus 0.45 mL; $p < 0.001$). When both BDM and calcium were included in the UW solution, calcium-stimulated ATP hydrolysis and contracture were prevented, left ventricular systolic pressure returned to 87% of control, and left ventricular diastolic volume and ATP content returned to control levels. Although the presence of calcium improves systolic performance, it also stimulates contracture and ATP hydrolysis, which is detrimental to extended myocardial storage. The presence of BDM protects the ischemic myocardium from calcium-stimulated ATP loss and the damaging effects of ischemic contracture. The addition of BDM and calcium to the UW solution significantly improves the quality of extended myocardial preservation by improving the heart's tolerance to cold ischemia.

(Ann Thorac Surg 1992;54:852–60)

Protection of the myocardium from ischemic damage has been an area of intense investigation. The development of hyperkalemic cardioplegic solutions proved that the heart could be made ischemic for brief periods with minimal morbidity [1]. In the transplantation arena, the clinical limits of 4 to 6 hours of cold storage were established in 1978 [2]. Since that time, methods of continuous perfusion or autoperfusion circuits have been proposed [3, 4] to extend the safe preservation time of the heart. Current clinical practice, however, remains with simple cold storage because it is proven effective and uncomplicated, and does not require more cumbersome equipment.

Principles governing the successful ischemic storage of solid organs such as the kidney, liver, or pancreas have been well described [5], and have led to the development of the University of Wisconsin (UW) solution. Application of these principles to heart preservation, however, has been less effective. We have recently reported that a fundamental difference exists between the heart and these other organs [6]. The myocardium is poorly tolerant to falling levels of adenine nucleotides during cold ischemic storage, and responds by developing an insidious contracture while in the arrested state (stone heart). Other intraabdominal organs lose their adenosine triphosphate (ATP) supply even faster than the heart and yet can endure prolonged periods of ATP exhaustion without structural or functional sequelae. We hypothesized that if myocardial energy depletion could be uncoupled from the resulting contracture, keeping the heart supple and relaxed, then improvement in prolonged preservation would be possible. In this study we experiment with 2,3-butanedione monoxime (BDM), which is a reversible inhibitor of contractile activity. We show that the addition of BDM and calcium to the UW solution dramatically improves the quality of myocardial preservation after 24 hours of cold storage.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Stringham, Department of Surgery H4/331, University of Wisconsin Hospitals and Clinics, 600 Highland Ave, Madison, WI 53792-3236.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Material and Methods

New Zealand white rabbits (1.8 to 2.3 kg) were used as the experimental animal, and were treated humanely in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research, the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institute of Health (NIH publication No. 85-23, revised 1985), and the guidelines of the Research Animal Review Committee of the University of Wisconsin, which reviewed and approved the experimental protocol.

Each rabbit was anesthetized with intravenous ketamine (50 to 75 mg), chemically paralyzed with intravenous pancuronium (1 mg), tracheostomized, mechanically ventilated, and administered 1,000 U of intravenous heparin. The heart was exposed by a median sternotomy, arrested in situ by an intravenous bolus injection of potassium chloride (4 mEq), and then quickly excised and placed in 4°C storage solution. A 6-mm (diameter) stainless steel cannula was secured in the aortic root, and the coronary circulation was flushed with 50 mL of the respective storage solution hung 50 cm above the heart. Pilot studies revealed perfusion pressures greater than 50 cm H_2O were damaging to the rabbit heart (data not shown). The ventricles were irrigated with clean storage solution through separate atriotomies, and the heart was immersed in storage solution in a plastic container, surrounded with crushed ice, and stored for 24 hours in a refrigerated room at 4°C.

Structural Analysis

The study was divided into two arms (Fig 1). The first was to study the structural and biochemical nature of the myocardium after storage but before reperfusion. Hearts in this arm were fitted with a left ventricular fluid-filled latex balloon secured with a pursestring stitch in the left atrial appendage. The balloon was connected to a pressure transducer by polyethylene tubing, and pressures were recorded on a Gilson multichannel physiograph recorder. Balloons were inflated to 1 mL 30 to 60 minutes after cold storage began (control) to allow for equilibration to temperature, and again after the 24-hour storage period. The pressure–volume relationship of the ventricle was assessed by calculating the change in pressure per balloon volume (dP/V) as:

$$dP/V = (P_p - P_c)/V_b,$$

where P_p = postpreservation pressure, P_c = control pressure, and V_b = balloon volume (1 mL). Balloons were created to approximate the volume of the rabbit ventricle and were found to be nearly completely compliant over the range of testing volumes [6].

The hearts were quickly sliced horizontally with a razor blade, and valvular and right ventricular tissue was removed. Left ventricular myocardial specimens were then immediately frozen in liquid nitrogen and stored at −70°C for later analysis of adenine nucleotides.

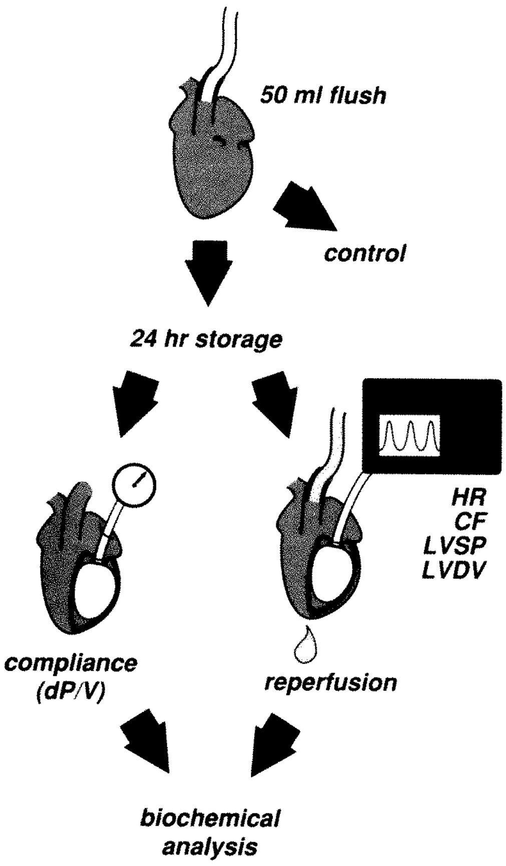


Fig 1. Schematic of experimental protocol. Rabbit hearts were flushed with University of Wisconsin solution (UW), UW + 1 mmol/L CaCl, UW + 30 mmol/L 2,3-butanedione monoxime (BDM), or UW + BDM and CaCl, and stored and studied as described in the Material and Methods section. (CF = coronary flow, dP/V = change in pressure–volume relationship [compliance]; HR = heart rate; LVSP = left ventricular systolic pressure, LVDV = left ventricular diastolic volume.)

Functional Analysis

In the second arm of the study, separate hearts were cold stored for 24 hours as described above, except balloon implantation and ventricular distention were omitted. After the preservation period, each heart was mounted on a modified Langendorff column for reperfusion with a modified Krebs-Henseliet buffer for analysis of function (Table 1). The column stood 120 cm in height, generating a static pressure (with the outflow occluded) of 90 mm Hg. With flow through the coronary circulation, diastolic perfusion pressure measured approximately 70 mm Hg. Aortic root pressure was monitored with an in-line pressure transducer, and the perfusate was warmed to 37°C with an in-line glass heat exchanger. Krebs-Henseliet buffer contained $NaHCO_3$, 25 mmol/L; KH_2PO_4, 1.2 mmol/L; NaCl, 118 mmol/L; KCl, 4.7 mmol/L; $MgSO_4$, 1.2 mmol/L; CaCl, 2 mmol/L; and dextrose, 10 mmol/L. After initiation of reperfusion, the initial 100 mL of Krebs-Henseliet buffer was discarded, and the perfusate was recirculated through an in-line 5-μm filter and bubbled with 95% O_2 and 5% CO_2, creating an oxygen tension of 450 to 600 mm Hg and a pH of 7.4. The

Table 1. Structural and Functional Data of Hearts After 24-Hour Cold Storage[a]

		Before Reperfusion	After Reperfusion			
Group	n	dP/V (mm Hg/mL)	HR (beats/min)	CF (mL/min)	LVSP (mm Hg)	LVDV (mL)
Control	6	. . .	209 ± 10.1	90.1 ± 10.9	136.5 ± 1.7	1.26 ± 0.04
UW	6	28 ± 10.4	183 ± 5.0[b]	47.7 ± 8.5[b]	57.0 ± 12.7[b]	0.45 ± 0.14[b]
UW + CaCl	6	81 ± 3.3[c]	173 ± 2.8[b]	56.6 ± 6.2[d]	78.3 ± 7.3[d]	0.47 ± 0.06[d]
UW + BDM	6	3 ± 1.4[c]	210 ± 7.7	54.3 ± 5.1[d]	101.5 ± 8.1[c]	0.87 ± 0.12[e]
UW + BDM + CaCl	6	2 ± 1.0[c]	236 ± 9.8[b]	63.1 ± 8.7[d]	118.3 ± 4.2[c,f]	1.29 ± 0.09[c,f]

[a] Structural data (dP/V) were obtained before reperfusion, whereas functional data were measured on separate hearts during 60 minutes of Langendorff reperfusion. Values shown represent the mean ± standard error for each group. [b] $p < 0.05$ versus control; [c] $p < 0.005$ versus UW; [d] p = not significant versus UW; [e] $p < 0.05$ versus UW; [f] p = not significant versus control.

BDM = 2,3-butanedione monoxime; CF = coronary flow; dP/V = change from control in left ventricular pressure–volume relationship (compliance); HR = heart rate; LVDV = left ventricular diastolic volume; LVSP = left ventricular systolic pressure; UW = University of Wisconsin solution.

hearts were reperfused immediately at systemic conditions of temperature and pressure, and no precaution was taken to limit reperfusion injury.

A fluid-filled latex balloon connected in-series to a Gould pressure transducer was placed into the left ventricle through a left atriotomy and secured to the aortic cannula. The balloon was inflated to 0.1 mL to monitor ventricular activity during the 60-minute reperfusion period, and further inflated for 5 minutes at 15-minute intervals, to create a measured end-diastolic pressure of 20 mm Hg. The pressure waveform was recorded on a Gould multichannel recorder, and left ventricular systolic pressure and heart rate were determined from the tracing. With the balloon inflated, coronary flow was determined by a 30-second collection of the effluent from the heart. The balloon volume necessary to create an end-diastolic pressure of 20 mm Hg was also recorded as an index of the left ventricular end-diastolic volume during reperfusion. Although not commonly measured in the isolated heart, this index proved to be a sensitive and reproducible indicator of diastolic relaxation upon reperfusion. The balloon did not remain inflated throughout the duration of reperfusion to minimize the risk of subendocardial ischemia, which might occur as a result of continuous pressure from the inflated balloon on the ventricular wall. The maximal function obtained during the reperfusion period was used for comparison between groups.

When reperfusion was completed, each heart was arrested with a bolus injection of KCl, removed from the column, quickly sliced horizontally to remove valvular and right ventricular tissue, frozen in liquid nitrogen, and stored at −70°C for later analysis of adenine nucleotides.

Biochemical Analysis

Myocardial adenylate content was determined by a modification of the technique described by Holliss and associates [7]. Frozen tissue samples were homogenized in 7% perchloric acid and centrifuged at 5,000 *g* for 10 minutes. The supernatant was neutralized with 2.4 mol/L Trizma base, centrifuge filtered through 0.45-μm Millipore filters, and analyzed for ATP, adenosine diphosphate, and adenosine monophosphate content with a Water's high-performance liquid chromatograph and Water's Resolve C-18 5-μm reverse-phase column. Total adenine nucleotide content was calculated as the sum of ATP + adenosine diphosphate + adenosine monophosphate. The precipitated pellet was resuspended in 10% deoxycholic acid and analyzed for protein content by the Biuret method [8] on a Shimadzu UV-160 spectrophotometer. Results were expressed as nanomoles of nucleotide per milligram of protein (Table 2). Each sample was processed in duplicate, and the results were averaged.

Experimental Groups

Preservation solutions were prepared and used within 24 hours (Table 3). Solutions were filtered through sequential 5-μm (Balston, Lexington, MA) and sterile 0.2-μm filters (Gelman Sciences, Ann Arbor, MI) into sterile bags and refrigerated at 4°C.

Control hearts were harvested, flushed with standard UW solution, and immediately reperfused for functional analysis. Three modifications of the UW solution were compared with standard UW after 24-hour storage: UW with addition of either 1 mmol/L CaCl or 30 mmol/L BDM, and UW with both 30 mmol/L BDM and 1 mmol/L CaCl added. Six or more hearts were analyzed for each solution in each arm of the study. Statistical analysis was performed with the aid of an Instat statistical software package (Graphpad Software, San Diego, CA). Data for each parameter have been expressed as a mean ± standard error. The mean of different groups was compared by a one-way analysis of variance, and significance was taken at p less than 0.05. Results were also calculated as a percentage of control for graphical presentation.

Results

Hearts stored for 24 hours in UW solution experienced a loss of ventricular compliance (Fig 2) and a reduction of ATP content to 38% of control (Fig 3). The addition of 1 mmol/L CaCl to the UW solution caused acceleration of ATP loss and a worsening of ventricular contracture. When 30 mmol/L BDM was added, there was no evidence of myocardial contracture during storage and ATP fell to

Table 2. Adenine Nucleotide Content Before and After Reperfusion in Hearts Cold Stored for 24 Hours[a]

Group	n	ATP (nmol/mg protein)	ADP (nmol/mg protein)	AMP (nmol/mg protein)	TAN (nmol/mg protein)
Before Reperfusion					
Control	6	27.9 ± 2.3	9.6 ± 1.3	2.3 ± 0.8	39.7 ± 2.3
UW	6	10.7 ± 1.0	12.5 ± 2.7	10.9 ± 1.4	34.1 ± 3.1
UW + CaCl	6	2.8 ± 0.6[b]	5.9 ± 0.8	18.5 ± 1.7	26.7 ± 2.6[c]
UW + BDM	6	15.7 ± 1.5[d]	11.2 ± 1.2	4.8 ± 0.8	31.7 ± 3.0[c]
UW + BDM + CaCl	12	17.1 ± 0.7[b]	11.2 ± 0.6	4.3 ± 0.5	32.6 ± 1.1[c]
After Reperfusion					
Control	6	13.4 ± 2.2	14.1 ± 1.0	8.8 ± 2.3	37.9 ± 3.5
UW	6	3.0 ± 0.9	5.3 ± 1.0	3.8 ± 0.7	12.0 ± 2.3
UW + CaCl	6	6.2 ± 1.1[c]	6.0 ± 1.0	3.0 ± 0.4	15.2 ± 2.1[c]
UW + BDM	8	12.4 ± 1.4[b,e]	9.8 ± 1.3	3.6 ± 1.0	25.8 ± 2.5[b]
UW + BDM + CaCl	7	13.6 ± 2.1[b,e]	10.9 ± 1.0	4.3 ± 0.4	28.8 ± 3.0[b]

[a] Rabbit hearts cold stored for 24 hours with either standard UW or UW modified with 30 mmol/L BDM, 1 mmol/L CaCl, or both. Adenylates were assayed by high-performance liquid chromatography either before or after reperfusion. Values shown represent the mean ± standard error for each group. Statistical significance calculated only for values of ATP and TAN: [b] $p < 0.005$ versus UW; [c] p = not significant versus UW; [d] $p < 0.05$ versus UW; [e] p = not significant versus control.

ADP = adenosine diphosphate; AMP = adenosine monophosphate; ATP = adenosine triphosphate; BDM = 2,3-butanedione monoxime; TAN = total adenine nucleotides; UW = University of Wisconsin solution.

only 56% of control level, significantly higher than storage in standard UW ($p < 0.05$). With both BDM and CaCl in the preservative, the calcium-induced acceleration of ATP loss was not seen, and the myocardium remained soft and compliant. Pre-reperfusion total adenine nucleotide content was not significantly different between any two groups, but hearts stored in the presence of BDM maintained a greater percentage as usable energy (ATP or adenosine diphosphate), whereas those hearts stored without BDM contained a greater percentage of adenosine monophosphate.

Functional analysis of the hearts confirmed the salutary effects of BDM in cold storage. All hearts spontaneously defibrillated upon reperfusion, and maximal function was usually attained by 30 to 45 minutes of reperfusion. Coronary flow decreased in all hearts studied, dropping lowest in hearts stored in UW solution to 53% of control (Fig 4). Hearts stored in UW solution with BDM and CaCl had slightly better coronary flow (70% of control); however, there was no statistically significant difference between any of the groups tested, and no correlation between coronary flow and other functional parameters. Heart rate decreased to 88% and 83% of control ($p < 0.05$) in hearts stored in UW solution and UW solution with CaCl, respectively (see Fig 4). Hearts stored in UW solution with BDM maintained heart rate at 104% of control, and those stored in UW solution with BDM and CaCl actually tended toward tachycardia (113% of control; $p < 0.05$).

The most beneficial effects of BDM and calcium were seen in examination of left ventricular systolic pressure (Fig 5) and diastolic volume (Fig 6). Hearts stored in UW solution regained only 42% of control left ventricular systolic pressure. The addition of CaCl improved left ventricular systolic pressure to 57% of control, despite

Table 3. University of Wisconsin Solution Composition[a]

Component	Concentration (mmol/L)
K-lactobionate	100
Raffinose	30
KH_2PO_4	25
Adenosine	5
$MgSO_4$	5
Glutathione	3
Allopurinol	1
Hydroxyethyl starch	50 g/L
Insulin	100 U/L
Dexamethasome	16 mg/L
TMP-SMZ	160 mg–32 mg/L

[a] pH adjusted to 7.4 with 25 mmol/L NaOH and KOH as needed; osmolarity, 320 ± 5 mOsm/L.

TMP-SMZ = trimethoprim sulfamethoxazole.

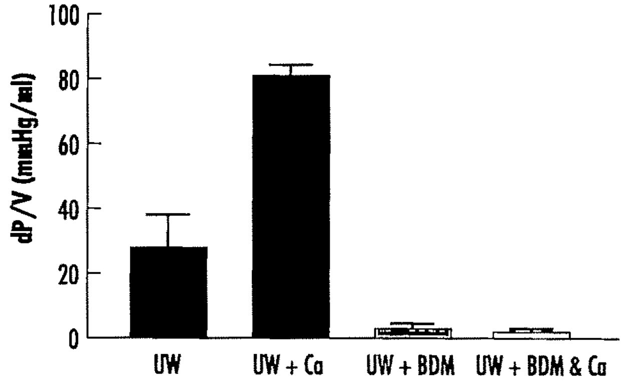


Fig 2. Change in left ventricular pressure–volume relationships after 24-hour cold storage as described in the Material and Methods section. (dP/V = change in ventricular pressure per balloon volume; other abbreviations are as in Figure 1.)

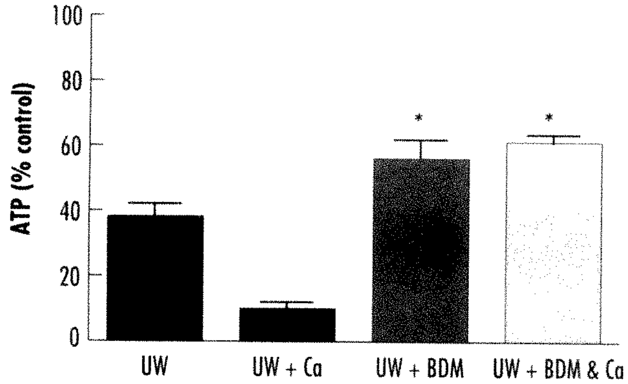


Fig 3. Left ventricular adenosine triphosphate (ATP) concentrations after 24-hour storage. Values represent the mean ± standard error of the mean for each group, calculated as a percent of control (100% = 27.9 nmol/mg protein). ($p < 0.05$ versus UW; abbreviations are as in Figure 1.)*

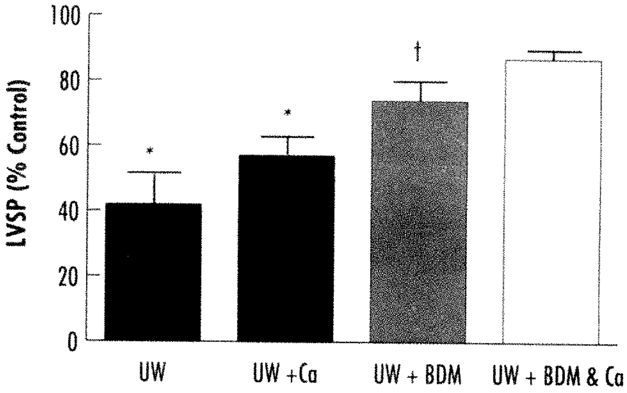


Fig 5. Left ventricular systolic pressure (LVSP) after 24-hour cold storage, calculated as a percent of control (100% = 136.5 mm Hg). ($p < 0.0005$; † $p < 0.05$; abbreviations are as in Figure 1.)*

development of severe contracture during storage. Both groups, however, developed severe impairment of diastolic relaxation upon reperfusion, regaining only 36% and 37% of left ventricular diastolic volume, indicating an inability to generate a cardiac output compatible with life. Hearts stored in UW solution with BDM, which remained compliant during storage, regained 74% of left ventricular systolic pressure ($p < 0.005$ versus UW) but also suffered diastolic dysfunction upon reperfusion. These hearts developed only 69% of control left ventricular diastolic volume, although this was less dysfunction than in those stored in standard UW solution ($p < 0.05$). Conversely, hearts stored in UW solution with both BDM and CaCl maintained 87% of left ventricular systolic pressure and 100% of left ventricular diastolic volume ($p < 0.0005$). The elimination of diastolic dysfunction and ventricular contracture on reperfusion by the addition of calcium is reminiscent of the calcium paradox phenomenon.

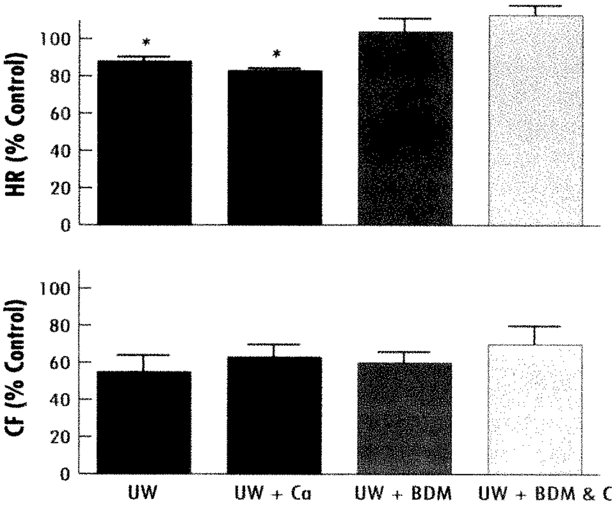


Fig 4. Heart rate (HR) and coronary flow (CF) of hearts cold stored 24 hours and reperfused 60 minutes as described in the Material and Methods section. Values reflect the mean ± standard error of the mean for each group, calculated as a percent of control (100% = 209 beats/min [HR] and 90.1 mL/min [CF]). ($p < 0.05$; abbreviations are as in Figure 1.)*

After 60 minutes of reperfusion, the myocardial ability to regenerate adenine nucleotides (see Table 2) was severely depressed after storage in UW solution or UW solution with CaCl, and ATP levels returned to only 22% and 46% of control, respectively (Fig 7). Hearts stored in the presence of BDM or BDM and CaCl regained 93% and 100%, respectively, of control ATP content. The ability of these hearts to regenerate adenine nucleotides corresponded closely with the ability to regain function.

Comment

Contracture of the myocardium has long been recognized as a deleterious event which heralds the presence of ischemic damage [9]. It has been shown to correspond to falling levels of myocardial ATP, and is thought to occur from actin-myosin rigor complexes which form between myofibrils, as molecules of ATP necessary for relaxation become unavailable [10]. Others have suggested that the energy-depleted ischemic myocyte, no longer capable of energy-dependent calcium compartmentation, experi-

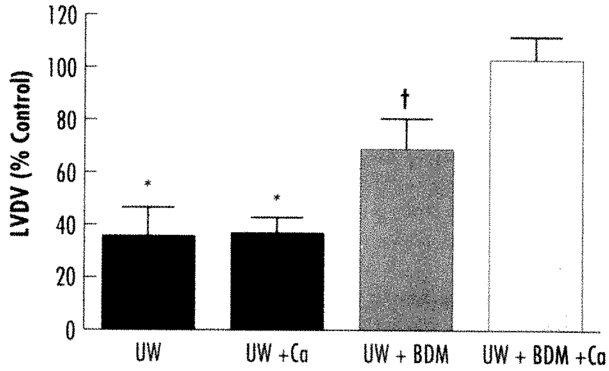


Fig 6. Left ventricular diastolic volume (LVDV) after 24-hour cold storage calculated as a percent of control (100% = 1.26 mL). ($p < 0.0005$; † $p < 0.05$; abbreviations are as in Figure 1.)*

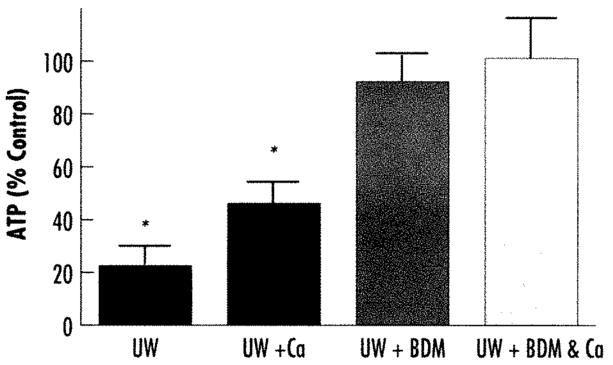


Fig 7. Myocardial adenosine triphosphate (ATP) regeneration after 24-hour cold storage and 60 minutes of isolated reperfusion, calculated as a percent of control (100% = 13.4 nmol/mg protein). ($p < 0.05$; abbreviations are as in Figure 1.)*

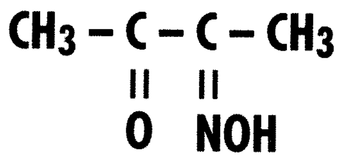
ences a rise in intracellular calcium which then stimulates contracture and further ATP depletion at the myofibrillar level, producing a progressive rigor [11]. We have previously shown that the development of contracture during extended cold storage is directly related to depletion of ATP supplies, and parallels the decline in myocardial contractile function [6]. This phenomenon of contracture is unique to the heart due to its muscular nature. Other organs such as the kidney and liver, which can be successfully stored for extended periods, suffer near exhaustion of ATP reserves very early during storage but remain completely viable. We hypothesized that storage of the heart could become more similar to that of other organs if ATP depletion could be reversibly uncoupled from the dire consequence of this energy-depletion contracture.

2,3-Butanedione monoxime, also known as diacetyl monoxime, is a compound of the oxime class initially investigated as an antidote for poisoning with organophosphate cholinesterase inhibitors [12]. Cholinesterases and plasma ali-esterases become inactivated by phosphorylation by the nerve agent, and are reactivated by the oxime acting as a chemical phosphatase [13]. More recently, BDM was found to inhibit actin-myosin cross bridge formation, and has been used as an experimental tool to dissociate contracture from other phenomena associated with ischemia [14].

Although the precise mechanism of BDM has not been well elucidated, studies have shown that its action seems to be primarily on the myofibrils, causing a dose-dependent decrease in the myofibrillar sensitivity to calcium-stimulated contraction [15]. Calcium binding to troponin C has been shown to be unaffected by BDM [16], suggesting its inhibitory effect may be on the myosin molecule itself. Higuchi and Takemori [17] have presented confirming evidence of this mechanism by showing a decrease in the myosin ATPase activity caused by BDM. This mechanism would result in preservation of ATP, and an actin-myosin complex that could not associate and contract. The myocardium would thus remain supple and relaxed despite contractile stimulation from free sarcoplasmic calcium or falling ATP levels. In this study we have observed both ATP preservation and inhibition of contracture during ischemia, supporting this proposed site of action. Whether BDM's chemical effect is that of a phosphatase or another reaction such as direct receptor antagonism has not been determined. Other actions of the molecule have been described, however, and may be important in its ischemic protection. These include a calcium-depleting effect on the sarcoplasmic reticulum [15] and a decrease in transsarcolemmal calcium currents [18]. A key factor in the effectiveness of BDM is its small (molecular weight, 101.1), uncharged (Fig 8), lipophilic nature, which allows penetration into and out of the intracellular milieu by a simple flush, thus creating a completely reversible contractile inhibitor for use during preservation.

In this study, we have shown that inclusion of BDM in the UW solution markedly improves the ischemic tolerance of the rabbit heart. We found that hearts stored with BDM under conditions of clinical allograft storage experienced less depletion of ATP reserves, completely avoided contracture during storage, developed better systolic function and less diastolic dysfunction, and regenerated substantially higher levels of ATP upon reperfusion. These hearts also developed a faster intrinsic rate when exposed to BDM and CaCl during storage, suggesting excellent preservation of the conduction system. Although inhibition of the contractile apparatus might protect from structural myocardial injury, improvement in multiple functional parameters as we have observed might indicate effects on multiple sites, such as membrane channels and mitochondria. Although our data suggest that BDM decreases ATP hydrolysis, other reports have shown no energetic advantage of exposure to BDM during ischemia [19]. These studies were performed with shorter periods of warm ischemia in cultures of isolated myocytes, and may not accurately represent events under hypothermic storage conditions in the intact heart. The action of BDM has also been shown to be potentiated at colder temperatures [16], making the study of this compound under conditions duplicating those experienced clinically to be even more important.

Our data also testify to the importance of calcium in myocardial storage solutions. Previous reports have shown that hearts perfused with a calcium-free solution suffer severe damage upon reperfusion with a calcium-containing solution, exhibiting loss of contractility, severe contracture, loss of intracellular proteins, and profound depletion of ATP [20]. This so-called calcium paradox was found to be inhibited by hypothermia [21]; however, increasing numbers of reports agree that postischemic



$$\begin{array}{ccccccc} CH_3 & - & C & - & C & - & CH_3 \\ & & \| & & \| & & \\ & & O & & NOH & & \end{array}$$

Fig 8. Chemical structure of 2,3-butanedione monoxime (molecular weight = 101.1).

myocardial function is improved by the inclusion of calcium in the perfusate or cardioplegia [22], even under hypothermic conditions. We have demonstrated that despite its protective capability, calcium can also be detrimental to extended preservation by inducing accelerated ATP hydrolysis and more severe myocardial contracture. With the inclusion of BDM, the damaging effects of calcium are inhibited, allowing its safe use for its protective properties alone. In fact, examination of the hearts stored in the presence of BDM with and without calcium reveals that systolic, diastolic, and metabolic function were all markedly improved by the simple addition of calcium. Although we did not measure enzyme release in this model, it may be that a small but significant degree of the calcium paradox does in fact occur under hypothermic conditions, and becomes increasingly prevalent with more prolonged intervals of cold ischemia.

The UW solution was used as the basis for our preservative because it has been shown to be superior to many other solutions for myocardial preservation in several experimental models [23–25], has been shown to be safe and equal to or better than currently used storage solutions in several clinical trials [26, 27], and is currently in use in several heart transplant programs, including our own. However the UW solution, in its present form, will not accomplish our goal of extended preservation by cold storage (24 to 48 hours) due to the onset of myocardial contracture at 12 to 18 hours of storage [6]. If clinical storage of the cardiac allograft is to be kept simple and uncomplicated, then this goal will only be attained with modifications such as those we have presented, which will tailor the solution to existing principles of preservation unique to the heart.

Despite our encouraging results, there are limitations to our model that should be addressed. This model is relatively inexpensive and uncomplicated, resulting in a high degree of reproducibility when performed by laboratory personnel, leaving little opportunity for error and allowing experimentation on a large number of variables. In addition, measurement of the left ventricular diastolic volume provides an accurate and reproducible estimation of left ventricular diastolic relaxation and dimensions. Diastolic dysfunction is an important indicator of myocardial damage occurring during the ischemic arrest period, which only becomes manifest when energy demand increases and the heart begins to function. Nevertheless, this remains a small animal nonworking model of heart transplantation. Due to reperfusion in a rather aphysiologic environment, substantial damage occurs to the isolated heart, which causes a progressive decline in function. This is readily apparent when comparing control hearts in this study before and after reperfusion. Adenosine triphosphate levels fell from 27.9 to 13.4 nmol/mg protein after 60 minutes of isolated reperfusion, despite only minor ischemia and continuous oxygenated reperfusion. Although our model gives valuable information concerning myocardial preservation, this promising compound (BDM) should also be studied in a large animal, blood-reperfused, working or orthotopic model for definitive determination of cardiac allograft viability. Such models are now being developed in our laboratory.

The concept of contracture inhibition with BDM is new to myocardial protection, and allows much more effective preservation of the ischemic heart. Application of this principle to intraoperative cardioplegia systems will also undoubtedly provide improved myocardial protection. 2,3-Butanedione monoxime retards ATP depletion, inhibits contracture due to energy depletion, allows use of calcium without risk of accelerated ATP hydrolysis, and improves postischemic function and ATP regeneration. Although further research is needed, the modification of the UW solution with BDM and CaCl creates an effective preservative for 24-hour cold storage of the rabbit heart and constitutes a substantial advance in improving myocardial tolerance to cold ischemia.

Supported by a grant from the University of Wisconsin Surgical Associates.

References

1. Gay WA Jr, Ebert PA. Functional, metabolic, and morphologic effects of potassium-induced cardioplegia. Surgery 1973;74:284–8.
2. Thomas FT, Szentpetery SS, Mammana RE, Wolfgang TC, Lower RR. Long-distance transportation of human hearts for transplantation. Ann Thorac Surg 1978;26:344–50.
3. Adachi H, Fraser CD, Kontos GJ. Autoperfused working heart-lung preparation versus hypothermic cardiopulmonary preservation for transplantation. J Heart Transplant 1987;6:253–60.
4. Wicomb WN, Collins GM. 24-hour rabbit heart storage with UW solution. Transplantation 1989;48:6–9.
5. Belzer FO, Southard JH. Principles of solid-organ preservation by cold storage. Transplantation 1988;45:673–6.
6. Stringham JC, Southard JH, Hegge J, Triemstra L, Fields BL, Belzer FO. Limitations of heart preservation by cold storage. Transplantation 1992;53:287–94.
7. Hollis DG, Humphrey SM, Morrison MA, Seelye RN. Reverse phase HPLC for rapid, comprehensive measurement of nucleotides, nucleosides, and bases of the myocardial adenine pool. Anal Lett 1984;17:2047–65.
8. Gornall AG, Bardewill CJ, David MM. Determination of serum proteins by means of the Biuret reaction. J Biol Chem 1949;177:751–66.
9. Cooley DA, Reul GJ, Wukasch DC. Ischemic contracture of the heart: "stone heart." Am J Cardiol 1972;29:575–7.
10. Hearse DJ, Barlick PB, Humphrey SM. Ischemic contracture of the myocardium: mechanisms and prevention. Am J Cardiol 1977;39:986–93.
11. Barry WH, Peeters GA, Rasmussen CAF Jr, Cunningham MJ. Role of changes in $[Ca^{2+}]_i$ in energy deprivation contracture. Circ Res 1987;61:726–34.
12. Askew BM. Oximes and hydroxamic acids as antidotes in anticholinesterase poisoning. Br J Pharmacol 1956;11:417–23.
13. Myers DK. Mechanism of the prophylactic action of diacetyl monoxime against sarin poisoning. Biochem Biophys Acta 1959;34:555–7.
14. Naylor WG, Elz JS, Buckley DJ. Dissociation of hypoxia-induced calcium gain and rise in resting tension in isolated rat hearts. Am J Physiol 1988;254:H678–85.
15. Horiuti K, Higguchi H, Umazume Y, Konishi M, Okazaki O, Kurihara S. Mechanism of action of 2,3-butanedione 2-monoxime on contraction of frog skeletal muscle fibers. J Muscle Res Cell Mot 1988;9:156–64.
16. Gwathmey JK, Hajjar RJ, Solero RJ. Contractile deactivation and uncoupling of crossbridges: effects of 2,3-butanedione

monoxime on mammalian myocardium. Circ Res 1991;69: 1280–92.
17. Higuchi H, Takemori S. Butanedione monoxime suppresses contraction and ATPase activity of rabbit skeletal muscle. J Biochem 1989;105:638–43.
18. Coulombe A, Lefevre IA, Deroubaix E, Thuringer D, Coraboeuf E. Effect of 2,3-butanedione 2-monoxime on slow inward and transient outward currents in rat ventricular myocytes. J Mol Cell Cardiol 1990;22:921–32.
19. Armstrong SC, Ganote CE. Effects of 2,3-butanedione monoxime (BDM) on contracture and injury of isolated rat myocytes following metabolic inhibition and ischemia. J Mol Cell Cardiol 1991;23:1001–14.
20. Zimmerman ANE, Daems W, Hulsmann WC, Snijder J, Wisse E, Durrer D. Morphological changes of heart muscle caused by successive perfusion with calcium-free and calcium-containing solutions (calcium paradox). Cardiovasc Res 1967;1:201–9.
21. Baker JE, Bullock GR, Hearse DJ. The temperature dependence of the calcium paradox: enzymatic, functional, and morphological correlates of cellular injury. J Mol Cell Cardiol 1983;15:393–411.
22. Jynge P, Hearse DJ, Braimbridge MV. Myocardial protection during ischemic cardiac arrest: a possible hazard with calcium-free cardioplegic infusates. J Thorac Cardiovasc Surg 1977;73:848–55.
23. Swanson DK, Pasaoglu I, Berkoff HA, Southard JA, Hegge JO. Improved heart preservation with UW preservation solution. J Heart Transplant 1988;7:456–67.
24. Elbeery JR, Lucke JC, Speier R, Rankin JS, VanTrigt P. Analysis of myocardial function in orthotopic cardiac allografts after prolonged storage in UW solution. J Heart Lung Transplant 1991;10:527–36.
25. Fremes SE, Li R, Weisel RD, Mickle DAG, Tumiati LC. Prolonged hypothermic cardiac storage with University of Wisconsin solution: an assessment with human cell cultures. J Thorac Cardiovasc Surg 1991;102:666–72.
26. Stein DG, Drinkwater DC Jr, Laks H, et al. Cardiac preservation in patients undergoing transplantation: a clinical trial comparing University of Wisconsin solution and Stanford solution. J Thorac Cardiovasc Surg 1991;102:657–65.
27. Jeevanandam V, Barr ML, Auteri JS, et al. University of Wisconsin solution versus crystalloid cardioplegia for human donor heart preservation: a randomized blinded prospective trial. J Thorac Cardiovasc Surg 1992;103:194–9.

DISCUSSION

DR ANDREW S. WECHSLER (Richmond, VA): I think this is a very nicely performed study. I have a few questions for you. I think it is impossible to assess systolic function when you have unequal diastolic performance for which you have not corrected. Because of the way that you assess diastolic function using pressure, you were unable to assess systolic function unless you did it over a series of diastolic volumes in the way that we conventionally would assess systolic function; because you did not assess intensity of contraction at some known end-diastolic fiber length. Thus, I think you have to allow in your interpretation of the data the possibility that there may have been a dichotomous effect, one on systole and one on diastole, or at least to consider it, perhaps, in your discussion.

I would take issue with the idea that you may have avoided a calcium paradox, because there is quite a bit of calcium in UW solution, which is usually attached to the impermeants. To get calcium paradox you have to have a virtually nil calcium concentration in the solution. It is an interesting hypothesis, but I do not know that the data support it.

Finally, your hypothesis, as I understand it, is that by inhibiting contracture you are able to reduce the rapid utilization of ATP that occurs when contracture is induced by ischemia. Is it possible that the drug is predominantly a myocardial depressant? Almost any myocardial depressant added to a preservative solution will enhance the effectiveness of the preservation technique that you are using. I assume that it is washed out when you reperfuse. Did the presence of that compound influence the rate, or the time that it took for the hearts to arrest before the storage interval? That would be another important consideration.

I think it is a very interesting compound and I think you are exactly right to try it in this manner, but I am curious to know some of these other characteristics.

DR STRINGHAM: You are exactly correct about the change in the systolic versus the diastolic properties of the muscle fibers. One of the things we tried to delineate in this study by measuring the diastolic ventricular volume was the degree of contracture occurring on reperfusion and how this would affect the systolic function of these hearts. It is very difficult to separate the two. So what we quantitated in this study was the amount of contracture occurring on reperfusion and then the systolic properties of that heart at a constant end-diastolic pressure. But you are right that there may be some difference in systolic properties just because of the impaired diastolic relaxation. However, in this study we did find that hearts that were stored in the presence of BDM and calcium did not undergo any contracture at all on reperfusion, and they were very similar to hearts that were immediately reperfused.

Concerning your comments about calcium in the UW solution, the standard UW solution as it comes packaged does not contain calcium, although calcium may be present as a contaminant of processing. We added calcium to the solution because we thought initially that many solutions that contain calcium actually provide better preservation and better postischemic function of the heart. We found, however, that these hearts underwent a dramatic acceleration of ATP depletion and contracture during storage. This phenomenon led us to seek something that would actually inhibit contracture from occurring despite the depletion of ATP.

Your comment about myocardial depressants is correct, and BDM is in fact a very potent depressant in the heart. The unique characteristic of BDM is that it acts primarily on the myofibrils. From what we have been able to understand, BDM does not allow the actin and myosin molecules to associate at all. Therefore, when ATP begins to be depleted, contracture is prevented by the addition of BDM. But you are right, this is a very strong myocardial depressant.

These hearts were harvested by giving a bolus injection of potassium chloride to the rabbits. So they were all arrested in the same way. The hearts were then flushed with the storage solution after they had been excised. However, a solution containing BDM would probably arrest a heart slightly faster than a hyperkalemic cardioplegic solution.

DR RAYMOND CARTIER (Montreal, Que, Canada): I would like to congratulate Stringham and associates for their excellent report and ask a single question. Did you use a freshly made UW solution or the commercial one? I am asking this question because of the potential harmful effect of the reduced glutathione contained in the shelf-stored UW solution as reported by Wilkins and Collins in one of their recent publications. With time, the reduced glutathione tends to get oxidized, and oxidized glutathione activates the collagenolytic system and then could contribute to myocyte damage.

Is it something that you took into account, or did you just assume that this was not really important?

DR STRINGHAM: We are aware of that article and its important concept. We use the UW solution not only experimentally but also clinically in heart preservation. For this study we made all of our UW solution from scratch in our laboratory within 24 hours of use. Clinically, when we use the UW solution, we add fresh reduced glutathione to it immediately before procurement. The concept that oxidized glutathione can cause some myocardial damage is an important observation.

DR ADNAN COBANOGLU (Portland, OR): If there is no further discussion, will you please close.

DR STRINGHAM: I have very little to add other than, as I said, we are very encouraged by this compound and its result on improving the postischemic function of the myocardium. Its mechanism of action on the heart has not been well elucidated yet, and much further study needs to be done on this compound to find out exactly what it does in the myocardium, and how its effects are beneficial to the heart.

Notice From The Society of Thoracic Surgeons

The Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons will be held at the San Antonio Convention Facility in San Antonio, Texas, January 25–27, 1993. There is no registration fee for the meeting for members of The Society. The registration fee is also waived for speakers, residents, and fellows. A $250.00 guest registration fee will apply to all other nonmember physicians.

The Twenty-sixth Postgraduate Course is scheduled for Sunday, January 24, 1993. The registration fee is $65.00 for all attendees. The Postgraduate Program will include minisymposia dealing with Thoracoscopy, Current Pulmonary Surgical Problems, Decisions in Cardiac Surgery, and Transplantation. A C.C.C.E.T.S. Basic Science Lecture and a special luncheon presentation by Floyd Loop on a subject of general interest will also be included.

In addition to the Postgraduate Program, this year's Annual Meeting will include a scientific poster session, breakfast seminars, the annual movie night, a wide range of surgical exhibits, and a complete schedule of scientific presentations drawn from the largest volume of abstracts ever submitted for presentation to The Society.

An advance program information booklet will be mailed to all members of The Society this fall. It will include a detailed schedule of events as well as registration and housing forms and other pertinent information regarding the Annual Meeting. Nonmembers wishing to receive the advance program booklet should write to the Secretary of The Society, Richard P. Anderson, MD.

Richard P. Anderson, MD
Secretary
The Society of Thoracic Surgeons
401 N Michigan Avenue
Chicago, IL 60611
(312) 644-6610
FAX (312) 527-6635

Extracorporeal Membrane Oxygenation for Cardiac Failure After Congenital Heart Operation

Stanley Ziomek, MD, James E. Harrell, Jr, MD, James W. Fasules, MD,
Sherry C. Faulkner, CCP, Carl W. Chipman, RN, Michele Moss, MD,
Elizabeth Frazier, MD, and Stephen H. Van Devanter, MD

Departments of Cardiothoracic Surgery and Pediatric Cardiology, David M. Clark Cardiovascular Center, Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, Arkansas

Despite continuing improvement in myocardial protection and surgical technique, the repair of complex congenital heart lesions can result in cardiopulmonary compromise refractory to conventional therapy. In a 29-month period, 24 patients (aged 14 hours to 6 years) were treated with extracorporeal membrane oxygenation (ECMO) 28 times for profound cardiopulmonary failure. Four patients required ECMO after each of two cardiopulmonary bypass procedures. Seventeen patients required ECMO to be initiated in the operating room: 12 (71%) were weaned successfully from ECMO, and 8 (47%) survived. Seven patients had ECMO initiated in the intensive care unit: 6 (86%) were weaned, and 5 (71%) survived. Serial echocardiograms demonstrated substantial recovery of cardiac function in 18 of 21 instances (86%) of ventricular failure from myocardial dysfunction. Overall, 18 of 24 patients (75%) were successfully weaned from ECMO including all 4 who underwent 2 ECMO treatments. We conclude that ECMO can successfully salvage children who have serious cardiopulmonary failure immediately after a congenital heart operation and that long-term survival is possible after two ECMO treatments.

(Ann Thorac Surg 1992;54:861–8)

Extracorporeal membrane oxygenation (ECMO) has become accepted therapy for children with acute respiratory failure refractory to maximal medical treatment [1–5]. In spite of continuing improvements in myocardial protection and operative technique, 80% of the operative mortality of congenital heart operations is caused by myocardial dysfunction or pulmonary hypertension [6–13]. The use of ECMO as lifesaving treatment for profound postoperative pediatric cardiac failure is increasing [4, 5, 14–23] and represents 4% of all ECMO cases [24]. We report our experience with 24 children treated with ECMO for postoperative cardiopulmonary failure after a congenital heart operation, the majority of whom had ECMO initiated in the operating room (OR).

Material and Methods

Patient Population

Data were obtained from 28 ECMO courses performed in 24 patients at Arkansas Children's Hospital who underwent cardiopulmonary bypass procedures between March 1989 and June 1991 (Table 1). Twelve were male and 12 were female. The patients' ages ranged from 14 hours to 6 years (mean, 12.5 months), and weights ranged from 2.9 to 12 kg (mean, 5.7 kg). Extracorporeal membrane oxygenation was initiated if, in the opinion of the attending pediatric cardiologist and surgeon, death was imminent despite maximal conventional therapy (ie, unable to be separated from cardiopulmonary bypass or postbypass mean arterial blood pressure < 40 mm Hg, acidosis, and oliguria despite maximal inotropic and ventilatory support). Before committing to a course of ECMO in the OR, a search for a structural cause of cardiac failure was made with hemodynamic measurements and epicardial echocardiography. If no correctable structural defects were found, cardiopulmonary bypass was continued for 1 to 2 hours while the ECMO team was contacted and the machine was brought into the OR. If the patient's hemodynamics had not improved by this time, ECMO was initiated in the OR. Several patients have been salvaged by going back on bypass in the last 10 years. However in our recent experience, all patients unable to be weaned from bypass have ultimately required ECMO support. The predominant indications for ECMO were ventricular failure (23), pulmonary hypertension (6), and hypoxemia in (1). Two cases of ventricular failure were caused by refractory supraventricular tachycardia after Fontan procedures, 2 were due to volume restriction from small right ventricles after Rastelli procedures, and 1 was secondary to a left ventriculotomy made to close multiple ventricular septal defects. Two other cases of ventricular failure were caused by obliteration of the ventricular cavities from severe ventricular hypertrophy, one after repair of a truncus arteriosus (both ventricles) and another after reconstruction of pulmonary hypoplasia in a patient with Williams syndrome (right ventricle). A patient with tetralogy of Fallot, right pulmonary hypoplasia, and a congen-

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Van Devanter, Department of Cardiothoracic Surgery, Arkansas Children's Hospital, 800 Marshall, Little Rock, AR 72202.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Cases of Postoperative Extracorporeal Membrane Oxygenation

Patient No.	Age	Weight (kg)	Sex	Diagnosis	Operation	Cannula Site	ECMO Indication	ECMO Duration (h)	Interval to ECMO (h)	Weaned	Outcome	Comments
1	2 d	3.6	M	Mixed TAPVR	TAPVR repair	Neck	PH	109	OR	Yes	Alive	
2	7 d	3.1	M	HLH	Norwood procedure	Chest	PH	43	OR	No	Died	Died of myocardial failure; renal failure
3	14 h	2.9	M	HLH	Norwood procedure; cardiac transplant	Chest	VF	62	OR	Yes	Died	Died of sepsis; RV infarct; renal failure; cardiac transplant after Norwood procedure
4	5 y	12	F	SV; TGV	Fontan procedure	Chest	VF	123	OR	No	Died	Died of *Candida* pneumonia; postop refractory SVT; renal failure
5	15 h	3.6	M	CDH with TOF	Patch RVOT obstruction	Chest	Hypoxemia	179	OR	No	Died	Died of *Candida* pneumonia; renal failure
6	1 mo	3.1	M	SV; TGV; VSD	Stansel procedure; aortic arch repair; atrial septectomy	Neck	VF	147	OR	Yes	Died	Died of bilateral pulmonary infractions
7	6 mo	4.0	F	Pulmonary atresia; hypoplastic PA; VSD; ASD s/p central shunt	Takedown central shunt; Rastelli procedure; PA reconstruction; VSD, ASD repair	Neck	VF	123	OR	No	Died	Died of myocardial failure
8[a]	3 mo	4.4	M	Partial AVC; severe MR	AVC repair; MV replacement	Neck	VF	65	6	Yes	Alive	
9	9 mo	4.9	F	Complete AVC (type C); PDA	AVC repair; PDA ligation	Neck	PH	67	OR	Yes	Alive	
10	3 d	3.6	F	Mixed TAPVR	TAPVR repair	Neck	VF	55	OR	Yes	Alive	
11	3 w	3.8	M	Truncus arteriosis (type II); branch PA stenosis	Truncus repair	Chest	VF	56	8	Yes		Postop cavitary obliteration from biventricular hypertrophy "suicide ventricles"
				Stenosis of truncus repair	PA reconstruction	Chest	VF	41	OR	Yes	Died	Died of mediastinitis; required RV–PA conduit and ASD, VSD closure postop
12[a]	27 mo	11	M	Tricuspid atresia; extreme reactive airway disease; s/p Fontan	Revision Fontan with RA–RPA conduit	Chest	PH	87	3	Yes		
				s/p Fontan revision	Partial takedown Fontan; placement of central shunt	Chest	PH	92	OR	Yes	Alive	
13[a]	14 mo	9.5	F	TGV; VSD; reduced RV volume; PV stenosis; dextrocardia; sup-inf ventricles	Rastelli procedure; ligation BT	Neck	VF	169	18	Yes	Alive	

14	23 h	3.3	M	HLH	Norwood procedure	Chest	VF	43	OR	No	Died	Died of intracranial bleed
15[a]	2 mo	4.9	M	VSD; RVOT obstruction	VSD repair; infundibular resection	Chest	VF	17	2	No	Died	Died of myocardial failure; ECMO initiated after 45 min of cardiac massage after resuscitation from postop cardiac tamponade
16[a]	2 d	3	F	Pulmonary atresia with intact septum; PDA	Patch RVOT; central shunt; PDA ligation	Chest	VF	69	2	Yes	Died	Died of *Staphylococcal* sepsis, site undetermined
17[a]	3 y	13	F	TGV; multiple VSDs; reduced RV volume	Rastelli procedure	Neck	VF	130	48	Yes		
				Multiple VSDs; TR s/p Rastelli procedure	Repair multiple VSDs; TV valvuloplasty	Chest	VF	65	OR	Yes	Alive	
18	3 y	12	M	Shone's complex; s/p MV replacement, s/p subaortic resection, s/p coarctation repair (in infancy)	Redo MV replacement; redo resection subaortic stenosis; aortic valvuloplasty	Chest	VF	198	OR	Yes	Died	Died of necrotizing *Pseudomonas* pneumonia
19[a]	6 y	16	F	Mitral atresia	Fontan procedure	Neck	VF	84	48	Yes	Alive	Postop refractory SVT; sepsis
20	9 d	3.5	F	HLH	Norwood procedure	Chest	VF	48	OR	Yes	Alive	Sepsis
21	18 mo	5	F	Williams syndrome; s/p aortic enlargement, s/p PA reconstruction	Redo reconstruction right and left PA branches	Neck	VF	170	OR	Yes	Alive	Postop cavitary obliteration from RV hypertrophy "suicide RV"
22	3 wk	3.8	M	Cor triatriatum; PAPVR	Cor triatriatum repair; PAPVR repair	Neck	PH	160	OR	Yes	Alive	
23	3 mo	4.9	F	Multiple VSDs; ASD; PDA	Repair multiple VSDs; ASD repair; PDA ligation	Neck	VF	198	OR	Yes	Alive	LV recovery began after 4 days of ECMO
24	17 mo	5.5	M	Partial AVC, severe MR; valvular and supravalvular PS	AVC repair; patch RVOT	Chest	VF	116	48	Yes		
				Recurrent MR s/p AVC repair s/p RVOT patch	Mitral valvuloplasty	Chest	VF	39	OR	Yes	Alive	

[a] Patient categorized as ECMO initiated in intensive care unit.

ASD = atrial septal defect; AVC = atrioventricular canal; BT = Blalock-Taussig shunt; CDH = congenital diaphragmatic hernia; ECMO = extracorporeal membrane oxygenation; HLH = hypoplastic left heart syndrome; LV = left ventricular; MR = mitral regurgitation; MV = mitral valve; OR = operating room; PA = pulmonary artery; PAPVR = partial anomalous pulmonary venous return; PDA = patent ductus arteriosus; PH = pulmonary hypertension; PS = pulmonary stenosis; PV = pulmonary valve; RA = right atrium; RPA = right pulmonary artery; RV = right ventricular; RVOT = right ventricular outflow tract; Shone's complex = mitral stenosis + subaortic stenosis + coarctation; s/p = status post; sup-inf = superior-inferior; SV = single ventricle; SVT = supraventricular tachycardia; TAPVR = total anomalous pulmonary venous return; TGV = transposition of great vessels; TOF = tetralogy of Fallot; TR = tricuspid regurgitation; TV = tricuspid valve; VF = ventricular failure; VSD = ventricular septal defect; Williams syndrome = supravalvular aortic stenosis + peripheral pulmonary artery stenosis.

ital diaphragmatic hernia was placed on postoperative ECMO support for hypoxemia.

Extracorporeal Membrane Oxygenation Technique

The ECMO circuit and technique used in our series were similar to those described by Bartlett and associates [1]. Venoarterial ECMO was used in all patients. Fifteen patients were cannulated through the chest via the right atrium and ascending aorta. Nine patients were cannulated through the neck using the right internal jugular vein and right common carotid artery. Anticoagulation was begun with 100 U/kg heparin (beef lung) and adjusted to keep the activated clotting time between 210 and 230 seconds. Platelet transfusions were given if the platelet count was less than 120 × 10^9/L (120,000/μL). The hematocrit was maintained greater than 0.40. In all patients, the sternum was left open and the wound covered with an iodinated plastic drape. Vancomycin and ceftazidime were used routinely for antibiotic prophylaxis. Every 48 hours, the wounds were cultured and then irrigated with an antibiotic solution. When necessary, clots were removed and bleeding points controlled with cauterization and a combination of thrombin spray and woven collagen. Patients were explored urgently to exclude tamponade for unexplained hypotension or increased central venous pressure.

Once the patient was on ECMO, vasopressors were reduced to maintain a mean blood pressure of 45 to 60 mm Hg with a central venous pressure less than 6 mm Hg. Extracorporeal membrane oxygenation flow rates were begun at 120 to 150 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Ventricular overdistention was minimized by maintaining the central venous pressure less than 6 mm Hg. The ventilator was set at an inspired oxygen fraction less than 0.40, tidal volume of 15 mL/kg, positive end-expiratory pressure less than 7 mm Hg, and a rate of 10 breaths/min. Patients were rolled from side to side every 8 hours to minimize atelectasis and pooling of secretions. Intravascular volume was maintained with packed red blood cell transfusions and colloid solutions. While on ECMO, diuresis was stimulated with furosemide or bumetanide to eliminate fluid overload and improve pulmonary gas exchange. An ultrafiltration device (Amicon filter; W.R. Grace Co, Beverly, MA) was added to the ECMO circuit if urine output decreased to less than 2 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ or if severe edema developed. The Sci-Med (Avecor, Minneapolis, MN) oxygenator was changed routinely every 7 to 9 days to lessen the risk of disseminated intravascular coagulopathy. The oxygen membrane was changed more frequently if necessary. The patients' hemodynamics and mixed venous oxygen saturations were monitored, and myocardial function was evaluated with epicardial echocardiography and direct visual inspection through the plastic drape. Cranial ultrasonography was performed daily in neonates to detect intracranial bleeding.

Criteria to begin weaning patients from ECMO included improved myocardial contractility on echocardiography, satisfactory pulmonary function, and reduced inotropic support. Over a period of 12 to 24 hours, ECMO flow rate was reduced to the minimum rated flow of the membrane oxygenator, which was 150 mL/min in the smaller patients. If the patients tolerated reduction of the flow rate, manifested by stable hemodynamics and arterial blood gases, they were given at least 1 hour of a trial off by diverting flow through the bridge of the circuit. Cannulas were flushed every 5 to 10 minutes to maintain patency during this period. If the patients maintained adequate hemodynamic and pulmonary function during the trial off, decannulation was performed. The carotid artery was repaired whenever possible, and the internal jugular vein was routinely ligated in patients decannulated from the neck. Sternal closure usually was delayed 2 to 3 days to allow for further diuresis and reduction of tissue edema, thereby reducing mediastinal compression.

Statistical Analysis

Data were presented as a range and mean or as a percentage of patients in a group. Differences between mean values were analyzed using Student's *t* test. An *F* test was performed to ensure equality of variances before the Student's *t* test was accepted. Differences of percentages between two groups were analyzed with Fisher's exact test. Two-tailed analyses were employed, and differences were considered statistically significant at the 95% confidence level ($p < 0.05$).

Results

Twenty-four patients underwent ECMO for postoperative cardiopulmonary failure. Of these, 4 patients underwent two separate treatments for a total of 28 ECMO courses. In 22 of the 28 courses (79%), weaning was successful. This represented 75% of the patients (18/24) receiving ECMO, of which 54% (13/24) were long-term survivors. Serial echocardiograms demonstrated substantial recovery in 18 of 21 (86%) instances of ventricular failure from myocardial dysfunction. Severe postoperative pulmonary hypertension unresponsive to conventional therapy was successfully reversed in all 6 patients (100%) with ECMO. The time from operation to institution of ECMO ranged from 0 to 48 hours (mean, 1.2 hours). Extracorporeal membrane oxygenation was initiated in the OR immediately after bypass in 17 patients (71%) of whom 12 were weaned and 8 were long-term survivors. Extracorporeal membrane oxygenation was started in the intensive care unit (ICU) in 7 patients, of whom 6 were weaned and 5 were long-term survivors. Four patients underwent two operations both of which required postoperative ECMO. All 4 were weaned successfully, and 3 were long-term survivors. The duration of ECMO ranged from 17 to 198 hours (mean, 96 hours).

The only factor that statistically decreased long-term survival of postoperative ECMO support was the development of an infectious complication (2/8 survived with infection versus 11/16 survived without infection; $p = 0.05$). All patients in whom fatal infections developed were cannulated through the chest (6/15 chest cannulations developed infection versus 0/9 neck cannulations; $p = 0.04$). Weight less than 5 kg or single ventricular anatomy tended to increase mortality of ECMO support but did not reach statistical significance. The incidence of infection was not influenced by the duration of ECMO, the age of the patient, or whether ECMO was started in the OR versus the ICU. Thirty-two percent of ECMO runs (6/19) started in the OR were complicated by infection compared with 22% (2/9) after ECMO initiated in the ICU (not significant; $p = 0.3$). There was a trend toward a lower salvage rate of patients who required ECMO support in the OR compared with patients whose condition deteriorated later in the ICU because patients who required ECMO support in the OR appeared to be at higher risk for operative death. Patients requiring ECMO in the OR weighed less than patients requiring ECMO later in the ICU (4.8 ± 2.8 kg in OR versus 8.9 ± 4.9 kg in ICU; $p < 0.05$) and underwent more complex operations (ECMO was initiated in the OR in all 4 Norwood procedures). At the time ECMO was discontinued, hypoxemia, a high mean airway pressure, or the requirement of an epinephrine drip were negative predictors of long-term survival ($p < 0.05$).

Deaths

Eleven patients (46%) died in this series. Seven deaths were early (on ECMO or shortly after decannulation) and four were late (>1 week after decannulation). The causes of death were infection (6), failure of myocardial recovery (3), pulmonary infarction (1), and intracranial hemorrhage (1). Of the 6 patients failing to be weaned from ECMO, 3 died of failure of myocardial recovery, 2 of *Candida* pneumonitis, and 1 of intracranial bleeding. Patient 2 was unable to be separated from cardiopulmonary bypass because of pulmonary hypertension and severe hypoxemia after a Norwood procedure. The patient did not improve and was taken off ECMO support because of progressive myocardial failure. Patient 3 underwent cardiac transplantation 24 hours after an unsuccessful Norwood procedure. The patient sustained a right ventricular infarction of the allograft with attempted sternal closure, had development of renal failure, and eventually died of gram-negative sepsis. Patient 4, who had been receiving antibiotics for refractory otitis media for 1 month before operation, had development of overwhelming *Candida* sepsis on ECMO. Patient 5 had severe right pulmonary hypoplasia secondary to a congenital diaphragmatic hernia, and had development of *Candida* pneumonitis on ECMO. Patient 6 was weaned from ECMO after a Damus-Kaye-Stansel procedure with a central shunt for a single ventricle. However, bilateral pulmonary infarctions developed related to temporary occlusion of the central shunt to avoid excessive pulmonary flow while on ECMO. A thrombectomy of the shunt and resection of a pneumatocoele were performed but the patient ultimately died. Patient 7 required ECMO support in the OR for biventricular failure after a Rastelli repair and pulmonary artery reconstruction for pulmonary atresia with hypoplastic pulmonary arteries. Extracorporeal membrane oxygenation was stopped after 123 hours of support for failure of myocardial recovery. Patient 15 underwent open cardiac massage for 45 minutes before initiation of ECMO. The patient was decannulated because no myocardial activity was demonstrated on echocardiography after 17 hours of support. Patient 14 was a newborn less than 24 hours old at the time of operation in whom intracranial bleeding developed after a Norwood procedure. The 4 patients who died late survived an average of 25 days before succumbing to infection. Deaths due to infection are discussed in the next section.

Complications

Fifteen complications developed in 11 patients (46%) in this series. Complications were infection (8), renal failure (4), right ventricular infarction (1), intracranial hemorrhage (1), and pulmonary infarction (1). Patients 4 and 18 had development of lethal pneumonitis (*Candida* and *Pseudomonas*) while on ECMO and had received long courses of antibiotics preoperatively for otitis media. Patient 16 had development of staphylococcal sepsis during ECMO support for right ventricular failure after operation for pulmonary atresia with an intact septum. Although the patient successfully recovered right ventricular function and was weaned from ECMO, the source of sepsis was not identified and the patient died 9 days later. Two other patients (19 and 20) had development of *Candida* sepsis from unidentified sources but eventually responded to amphotericin B and survived. Patient 11 had development of mediastinitis (*Staphylococcus aureus*) after repair of a stenotic right ventricle–pulmonary arterial conduit and was never able to be weaned from the ventilator because of persistent sepsis. Four patients were treated for renal failure while on ECMO, patients 2 and 5 with ultrafiltration, patient 3 with peritoneal dialysis, and patient 4 with hemodialysis. Two of the 4 patients with renal failure were weaned from ECMO, but all eventually died.

Mechanical Difficulties

Three mechanical problems occurred during the 28 ECMO courses in this series. Rupture of the pump-head tubing in the raceway occurred with the first patient in the series. Super Tygon tubing (Norton Performance Plastics, Akron, OH) was used in all patients afterward without incident. One shut-down of the ECMO circuit occurred because of a blown fuse in the pump computer. The faulty computer was replaced without coming off flow. A third patient sustained temporary dislodgement of an arterial cannula. None of these mechanical problems resulted in an adverse patient outcome.

Follow-up

Follow-up of the 13 survivors ranged from 1 month to 18 months with a mean of 7 months. Two patients required a subsequent cardiac operation, one a redo mitral valve replacement 10 months postoperatively, and the other a repair of a stenotic right pulmonary vein 7 months postoperatively. These defects were unlikely to have been responsible for the patients requiring ECMO postoperatively because neither was detected with repeated intraoperative and postoperative echocardiography and hemodynamic measurements, and because these defects became evident more than 6 months after hospital discharge. Both are doing well at home. One patient is on antiseizure medication and another is receiving amiodarone for chronic atrial flutter. At present all survivors have activity levels normal for age, although 2 have mild developmental delay.

Table 2. Extracorporeal Membrane Oxygenation for Cardiopulmonary Failure After Congenital Heart Operation (series with 10 or more patients reported)

Series	Total Patients	Weaned from ECMO	Long-Term Survival	OR ECMO Survival
Kanter et al, 1987 [18] (St. Louis Univ Med Center)	13	7 (54%)	5 (38%)	0/1
Weinhaus et al, 1988 [21] (St. Louis Children's Hosp)	13	8 (62%)	5 (38%)	0/4
Rogers et al, 1989 [19] (Univ Pittsburg Med Center)	10	8 (80%)	7 (70%)	0/1
Klein et al, 1990 [20] (Children's Hosp of Michigan)	39	22 (56%)	21 (54%)	2/9(22%)
ELSO Registry data (Oct 1991)	435	191 (44%)	N/A	N/A

ECMO = extracorporeal membrane oxygenation; ELSO = Extracorporeal Life Support Organization; N/A = not available; OR = operating room.

Comment

This study demonstrates ECMO can be used successfully in neonates and children for postoperative cardiopulmonary failure refractory to conventional medical therapy. Seventy-five percent of our patients (18/24) were weaned. The Extracorporeal Life Support Organization registry reported a 44% survival (weaned from ECMO) for postoperative cardiac patients [24]. Of the 18 patients weaned in this series, 13 (72%) were discharged home, representing a 54% overall survival rate. In comparison with previous reports [18–21], this series includes a majority of patients begun on ECMO in the OR (Table 2).

In our experience, long-term survival was best supporting myocardial dysfunction after repair of left to right shunts and severe pulmonary hypertension after repair of anomalous pulmonary venous return. Lowest patient survival with postoperative ECMO occurred after Norwood procedures.

Extracorporeal membrane oxygenation has allowed us to perform corrective repairs in several patients we considered to be at extreme risk for death. Preoperative catheterization in patients 13 and 17 with transposition of the great vessels and ventricular septal defect revealed relatively hypoplastic right ventricles. Both underwent Rastelli repairs and have done well. Extracorporeal membrane oxygenation support allowed for gradual improvement in diastolic right ventricular function and progressive enlargement of both patients' right ventricular chambers. Patient 9 had a complete atrioventricular canal and was transferred to our hospital at 9 months of age with severe pulmonary hypertension. After repair, the patient's suprasystemic pulmonary artery pressure was managed successfully with ECMO.

The intraaortic balloon pump [25, 26] and the left ventricular assist device [27, 28] have been used for myocardial dysfunction after congenital heart operations. However, both are limited to support of the left ventricle. Extracorporeal membrane oxygenation may be superior because it offers biventricular and pulmonary support and can be performed in neonates.

A high incidence of clinically significant hemorrhage with postoperative ECMO has been frequently reported [18–21] and has led to a reluctance to initiate support in the OR [19]. Our experience has shown life-threatening hemorrhage can be avoided as there were no instances of uncontrolled mediastinal hemorrhage. Factors found to be helpful in controlling hemorrhage were (1) platelet transfusions before initiation of ECMO, (2) meticulous surgical hemostasis, (3) liberal use of topical hemostatic agents, (4) a low threshold for mediastinal exploration, and (5) tight control of the activated clotting times. Long-term survival of patients with ECMO initiated in the OR was similar to that of patients requiring ECMO in the ICU. Another concern about the use of postoperative ECMO has been the need for venting the failing left ventricle [21, 29]. This was believed not to be necessary in any patients in this series. Ventricular overdistension was minimized by maintaining low central venous pressure, adequate venous outflow, and high ECMO flow rates.

Infection lowered ECMO salvage rate by 22%, causing 4 of 18 patients successfully weaned to eventually die: 2 of generalized sepsis secondary to an unidentified source, 1 of pneumonitis, and 1 of mediastinitis. Patients requiring postoperative circulatory support appear to be at higher risk for infectious complications for a variety of reasons including (1) open wounds postoperatively, (2) presence of central lines and ECMO cannulas, (3) prolonged endotracheal ventilation, (4) fungal and *Pseudomonas* overgrowth from prolonged preoperative and postoperative antibiotics, and (5) potential immunosuppression from prolonged cardiopulmonary bypass. Despite this, it appears that mediastinitis was effectively prevented, as there was only 1 case in 28 ECMO courses. After reviewing our results from this series, we are taking measures to lower ECMO mortality from infection. Elective operations are now delayed at least 1 month after administration of antibiotics has been stopped. We will be making an attempt in the future to close the sternum within 24 to 36 hours while the patient is on ECMO, as long as there is minimal mediastinal hemorrhage. Because candidemia developed in 4 patients, changes in our intravenous and topical antibiotics are being considered. In addition, we are setting up a protocol to investigate the effects of prolonged cardiopulmonary bypass on the immune system, with an emphasis on T-cell function in view of the high incidence of fungal infections. Finally, although a clear explanation for a high rate of infectious complications in patients cannulated in the chest is not apparent, neck cannulation is preferred if technically possible. We postulate that chest cannulation may have increased systemic infectious complications because the raw surfaces of the mediastinum were more difficult to keep sterile with cannulas exiting from the open chest than from a separate site in the neck.

Central shunts were occluded early in our experience to prevent excessive pulmonary flow. After the occurrence of bilateral pulmonary infarctions caused by occluding the central shunt, systemic to pulmonary flow through a shunt is now preserved but restricted. Several patients early in our experience were taken off ECMO when echocardiography showed no recovery of ventricular function after 12 to 24 hours. Presently, ECMO support is provided for patients without early ventricular recovery as long as progressive acidosis or multiorgan failure does not develop. Our 23rd patient did not show return of any noticeable ventricular function until the fourth day of ECMO support, and is a survivor with normal ventricular function.

In conclusion, ECMO has been a valuable resource in the management of postoperative cardiopulmonary failure refractory to optimal medical management after repair or palliation of congenital heart defects. Although late infection remains a serious risk, our willingness to initiate support earlier has grown as mechanical risks of postoperative ECMO for the most part have been avoided and benefits of early intervention have been observed. Extracorporeal membrane oxygenation can be used with good results in patients with profound postoperative cardiopulmonary failure in the OR and in those who require a second course of postoperative circulatory support.

References

1. Bartlett RH, Andrews AF, Toomasian JM, et al. Extracorporeal membrane oxygenation for newborn respiratory failure: forty-five cases. Surgery 1982;92:425–33.
2. Krummel TM, Greenfield LJ, Kirkpatrick BV, et al. Clinical use of an extracorporeal membrane oxygenator in neonatal pulmonary failure. J Pediatr Surg 1982;17:525–31.
3. Toomasian JM, Snedecor SM, Cornell RG, Cilley RE, Bartlett RH. National experience with extracorporeal membrane oxygenation for newborn respiratory failure: data from 715 cases. Trans Am Soc Artif Intern Organs 1988;34:140–7.
4. Trento A, Thompson A, Siewers R, et al. Extracorporeal membrane oxygenation in children. New trends. J Thorac Cardiovasc Surg 1988;96:542–7.
5. Redmond CR, Graves ED, Falterman KW, et al. Extracorporeal membrane oxygenation for respiratory and cardiac failure in infants and children. J Thorac Cardiovasc Surg 1987;93:199–204.
6. Kirklin JK, Castaneda AR, Kean JF, Fellows KE, Norwood WI. Surgical management of multiple ventricular defects. J Thorac Cardiovasc Surg 1980;80:485–93.
7. Mavroudis C, Weinstein G, Turley K, Ebert PA. Surgical management of complete atrioventricular canal. J Thorac Cardiovasc Surg 1982;83:670–9.
8. Arciniegas E, Farooki ZQ, Hakimi M, Perry BL, Green EW. Early and late results of total correction of tetralogy of Fallot. J Thorac Cardiovasc Surg 1980;80:770–8.
9. Castaneda AR, Trusler GA, Paul MH, Blackstone EH, Kirklin JW. The early results of treatment of simple transposition in the current era. J Thorac Cardiovasc Surg 1988;95:14–28.
10. Ebert PA, Turley K, Stranger P, Hoffman JEI, Heymann MA, Rudolph AM. Surgical treatment of truncus arteriosus in the first 6 months of life. Ann Surg 1984;200:451–6.
11. Mayer JE Jr, Helgason H, Jonas RA, et al. Extending the limits for modified Fontan procedures. J Thorac Cardiovasc Surg 1986;92:1021–8.
12. Meliones JN, Sider AR, Bove EL, Rosenthal A, Rosen DA. Longitudinal results after first-stage palliation for hypoplastic left heart syndrome. Circulation 1990;82:151–6.
13. Kirklin JW, Barratt-Boyes BG. Cardiac surgery. New York: Wiley Medical, 1986:514.
14. Soeter JR, Mamuja RT, Sprague AY, et al. Prolonged extracorporeal oxygenation for cardiorespiratory failure after tetralogy correction. J Thorac Cardiovasc Surg 1974;66:214–8.
15. Bartlett RH, Gazzaniga AB, Fong SW, Jefferies MR, Roohk HV, Haiduc N. Extracorporeal membrane oxygenator support for cardiopulmonary failure: experience in 28 cases. J Thorac Cardiovasc Surg 1977;73:375–86.
16. Galantowicz ME, Stolar CJH, King TC. Extracorporeal membrane oxygenation for perioperative support in pediatric heart transplantation. J Thorac Cardiovasc Surg 1991;102:148–52.
17. Bartlett RH, Gazzaniga AB, Wetmore NE, et al. Extracorporeal membrane oxygenation (ECMO) in the treatment of cardiac and respiratory failure in children. Trans Am Soc Artif Intern Organs 1980;26:578–8.
18. Kanter KR, Pennington G, Weber TR, Zambie MA, Braun P, Martychenko V. Extracorporeal membrane oxygenation for postoperative cardiac support in children. J Thorac Cardiovasc Surg 1987;93:27–35.
19. Rogers AJ, Trento A, Sievers RD, et al. Extracorporeal membrane oxygenation for postcardiotomy cardiac shock in children. Ann Thorac Surg 1989;47:903–6.
20. Klein MD, Shaheen KW, Whittlesey GC, et al. Extracorporeal membrane oxygenation for the circulatory support of children after repair of congenital heart disease. J Thorac Cardiovasc Surg 1990;100:498–505.
21. Weinhaus L, Canter C, Noetzel M, et al. Extracorporeal membrane oxygenation for circulatory support after repair of congenital heart defects. Ann Thorac Surg 1989;48:206–12.
22. Pennington DG, Merjavy JP, Codd JE, et al. Extracorporeal membrane oxygenation for patients with cardiogenic shock. Circulation 1984;70:130.
23. Registry Report of the Extracorporeal Life Support Organization, October 1991. Ann Arbor, MI: ECMO Data Registry, 1991.
24. Meliones JN, Custer JR, Snedecor SM, Moler FW, O'Rourke PP, Delius RE. Extracorporeal life support for cardiac assist in pediatric patients: review of ELSO Registry data. Circulation 1991;84:168–72.
25. Pollock JC, Charlton MC, Williams WG, Edmons JF, Trusler GA. Intraaortic balloon pumping in children. Ann Thorac Surg 1980;29:522–8.
26. Veasy LG, Blalock RC, Orth JL, Boucek MM. Intraaortic balloon pumping in infants and children. Circulation 1983;68:1095–100.
27. Karl TR, Sano S, Horton S, Mee RBB. Centrifugal pump left heart assist in pediatric cardiac operations. J Thorac Cardiovasc Surg 1991;102:624–30.
28. Drinkwater DC, Laks H. Clinical experience with centrifugal pump ventricular support at UCLA Medical Center. ASAIO Trans 1988;34:505–8.
29. Eugene J, McColgan SJ, Moore-Jeffries EW, Ott RA, Haiduc NJ, Roohk HV. Cardiac assist by extracorporeal membrane oxygenation with in-line left ventricular venting. ASAIO Trans 1984;30:98–102.

DISCUSSION

DR JOSEPH B. ZWISCHENBERGER (Galveston, TX): I rise to congratulate Dr Ziomek and the Little Rock group for their excellent results. I only want to mention that you referred to the ELSO Registry with a 44% initial weaning rate from ECMO. The same registry reports a 30% to 50% incidence of serious hemorrhagic complications in this particular subgroup of patients, and yet your abstract only mentions hemorrhagic complications in 1 patient. I do not recall your presentation focusing on those complications. I would like to hear how you manage your circuit, heparin dose and platelet use and whether or not you use Amicar in the management of your patients to have such an outstandingly low bleeding complication rate.

DR ZIOMEK: Thank you for your kind comments. Almost every patient in our series had some amount of oozing from the mediastinum while on ECMO, but no patient had development of exsanguinating hemorrhage or had to be discontinued from ECMO as a result of mediastinal hemorrhage. Factors that we believe have allowed us to minimize bleeding complications with postcardiotomy ECMO start with transfusing 1 to 2 units of platelets while the patient is on bypass immediately before initiation of ECMO. As the perfusionists set up the ECMO circuit in the OR, meticulous care is undertaken to stop all mediastinal oozing, paying particular attention to ensure that the venous and arterial cannula sites are very secure.

While the patients are on ECMO, we try to keep the platelet count greater than 120,000/μL and also follow the fibrinogen level very closely. We give 10 mL of cryoprecipitate if the fibrinogen level falls to less than 150. Also, and this is very important, we leave the sternum open on all patients while they are on ECMO to allow us to identify and control bleeding sites with electrocautery or thrombin and Surgicel. This also substantially lessens the chance of cardiac tamponade developing while the patient is receiving postcardiotomy ECMO support.

DR PETER P. McKEOWN (Tampa, FL): My compliments again for an excellent series. I wonder if you could expand on what you mentioned about the mediastinal bleeding and as it relates perhaps to the site of cannulation. You said your preference at the moment would be for neck cannulation, and I wonder if you could talk about problems that you have had with neck cannulation, size of cannulas and flow differences, as opposed to those that you cannulated directly.

DR ZIOMEK: I am going to defer to Dr Harrell.

DR HARRELL: Thank you, Dr Ziomek, and thank you for your comments, Dr McKeown. I thought I would elaborate just a little bit on some of the techniques that Dr Ziomek has not covered. For neck cannulation, we try to go with as small an arterial cannula as we can possibly put through the carotid artery in an effort to preserve the carotid for repair after decannulation. As a rule, we have not had serious problems with hemorrhage. If there is some oozing, it is usually from around the skin or the mediastinal tissues and is controlled with electrocautery or packed woven collagen. One of the reasons we like neck cannulation is it gets the cannulas out of the chest allowing better inspection of the heart and surgical field for hemostasis, if necessary. Achieving adequate pump flow through the neck cannulas has not been a problem.

In addition, the activated clotting times are controlled fairly tightly, between about 210 and 230 seconds, and we believe that this is a reasonable range of control for heparin titration to the point that we have not had serious problems with hemorrhage.

DR MICHAEL G. MORONT (Birmingham, AL): I have two questions for you. Number one, have you had any experience with the inability, during ECMO without a left atrial cannula, to decompress the left ventricle?

DR HARRELL: That is also a very good question. Certainly we have had concerns about that, but in our series and experience we have not seen serious problems. We temporarily attempted left ventricular decompression on 1 patient with a pulmonary artery cannula but we did not believe that it added anything to the overall support.

DR MORONT: What measures exactly do you use as criteria during your weaning from ECMO?

DR HARRELL: It is a combination of factors. The absence of acidosis, evidence of good or improving ventricular function by echocardiography, satisfactory visual inspection of the heart through the open chest, and improving hemodynamics are the usual criteria. We normally like to do a "trial-off" period of at least an hour or two. If the patient tolerates the trial-off ECMO successfully, and if we are all satisfied, including the cardiologists, then we proceed with decannulation.

DR THOMAS L. SPRAY (St. Louis, MO): I would like to again congratulate Dr Ziomek, Dr Harrell, and their associates on this series. This is a good result in terms of weaning and long-term survival, and it is also clear that if you look at the other reported series, the overall survival rates are getting to be about what you would expect with adult assist device technologies. This can be applied over a wide range.

My question has to do with the issue of the hypoplastic left heart syndrome and the Norwood operation. We have found that ECMO really is not very useful in this setting because most of the patients are in trouble either from too much or too little pulmonary blood flow, and putting fully oxygenated arterial blood back into the aorta often causes the pulmonary resistance to drop so low that they flood the ventricle no matter what the ECMO flow. So I am very interested in this concept of limiting the amount of flow through the shunt while the patient is on ECMO, and if you do that, how then would you manage taking the patient off ECMO? Do you partially release the limitation in shunt flow or do you take it off completely?

DR HARRELL: Dr Spray, thank you for your comments. First of all, our worst results were with the hypoplastic left heart patients and, I think, a lot of it has to do with the reactivity of the pulmonary vasculature. With the central shunt in place, all we do is take a metal Hemoclip and, watching the saturations and watching the hemodynamics, crimp down the clip to a point where we think we have reduced the pulmonary flow to a reasonable level and yet still maintain enough flow so that the shunt will not clot off, as occurred in 1 patient. Since we have started to restrict flow, we have only had 2 patients in whom we have tried to do this and, so far, it seems to have worked, as we were able to wean the patients off by completely removing the Hemoclip just before weaning. But we have had very limited experience with this technique so far.

DR JOHN TERRANCE DAVIS (Columbus, OH): I have a quick question about what percentage of your practice this represents: is this greater than 1 per month? I was also interested in how many open heart procedures this is and what percentage of that this represents.

DR HARRELL: In looking back over the series of about 2½ years, it roughly represents about 350 pumps, which would be somewhere around 6% or 7%. Now, some people may say that this is perhaps a little on the high side, but I think that in our setting where we do a lot of ECMO support for other reasons, we have felt very comfortable using ECMO as a route for support, and we think it really has helped tremendously from the standpoint of supporting the marginal patient in coming off bypass.

Coarctation of the Aorta in Infants: Does the Aortic Arch Grow After Repair?

John L. Myers, MD, Brian A. McConnell, BS, and John A. Waldhausen, MD

Division of Cardiothoracic Surgery, Department of Surgery, The Pennsylvania State University, The Milton S. Hershey Medical Center, Hershey, Pennsylvania

Infants with coarctation of the aorta frequently require a corrective operation during the first year of life. These patients frequently have a smaller than normal transverse aortic arch. Despite good repairs with different techniques, the proximal transverse aortic arch often remains smaller than normal. The hemodynamic molding theory predicts that growth of the aortic arch should occur when normal flow is established through the aortic arch. Preoperative and postoperative aortograms were reviewed in patients who underwent subclavian flap aortoplasty for the repair of coarctation. Patients were divided into two groups. Subclavian flap aortoplasty was performed at 1 month of age or earlier in group I, and at more than 1 month but less than 1 year of age in group II. Aortograms performed in patients without coarctation were used as age-matched controls (group III). The transverse aortic arch in groups I and II did grow and were compared with the control group. Group I patients achieved more growth than those in group II. No aortic arch gradients were present at postoperative follow-up.

(Ann Thorac Surg 1992;54:869–75)

Surgical repair of coarctation of the aorta in infants is usually accomplished by resection of the coarctation with end-to-end anastomosis or by subclavian flap aortoplasty (SFA). The incidence of recurrent coarctation has been greater in infants than in older children [1, 2]. To enlarge the anastomosis and allow growth potential, some surgeons use the SFA [3–6], whereas others use an extended end-to-end technique, resecting the coarctation and anastomosing the descending aorta to the underside of the aortic arch [7–10]. The SFA is a longitudinal repair at the coarctation site that allows circumferential growth of native tissue and the subclavian flap [11, 12]. Even though the coarctation site is repaired surgically, proximal regions of the aorta in the transverse aortic arch often remain small and, if growth does not occur, may require additional correction of the relative "stenosis" of the aortic arch. According to the hemodynamic molding theory it would be expected that these regions would grow postoperatively with a resultant increase in blood flow across the aortic arch. Our hypothesis is that when coarctation of the aorta is repaired early in life, the proximal aorta will grow. Our study was undertaken to test this hypothesis. Infants with tubular hypoplasia of the aortic arch proximal to the left subclavian artery require augmentation of their transverse aortic arch at the time of the initial operation and not simple end-to-end repair, SFA, or patch aortoplasty; therefore, these patients are not included in this series.

Material and Methods

We reviewed the hospital records of all infants whose coarctation of the aorta was repaired by SFA (n = 70). To assess the growth of the aortic arch after operation we analyzed the aortograms of all patients who had both a preoperative and postoperative aortogram (n = 17). Most of these patients were operated on early in our series; in recent years, the wide application of two-dimensional and color Doppler echocardiography has minimized the need for routine preoperative and postoperative aortograms in patients with coarctation.

The left anterior oblique projection of each aortogram was displayed on a screen and a tracing of the aortogram from the aortic annulus to the diaphragm was made. The left anterior oblique view minimizes the difference in magnification between the ascending and descending aorta by placing them in the same plane parallel to the radiographic image recorder. Measurements of the aortic diameter were made at six different regions on the tracing of each preoperative and postoperative aortogram (Figs 1A and 1B, respectively). The six sites included: region 1: proximal, mid, and distal ascending aorta; region 2: between the innominate and left carotid arteries; region 3: between the left carotid and left subclavian arteries; region 4: level of coarctation (repair site); region 5: just distal to the coarctation (repair site); and region 6: descending aorta.

The seventeen patients in this study were divided into two groups. Group I (n = 10) had SFA at the age of 1 month or younger, and group II patients (n = 7) had SFA after 1 month of age but before 1 year of age. Group III (n = 15) were patients who had aortograms while undergoing cardiac catheterization for the diagnosis of congenital heart defects that did not include patent ductus arteriosus

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Myers, Division of Cardiothoracic Surgery, Department of Surgery, Penn State Children's Hospital, The Milton S. Hershey Medical Center, PO Box 850, Hershey, PA 17033.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

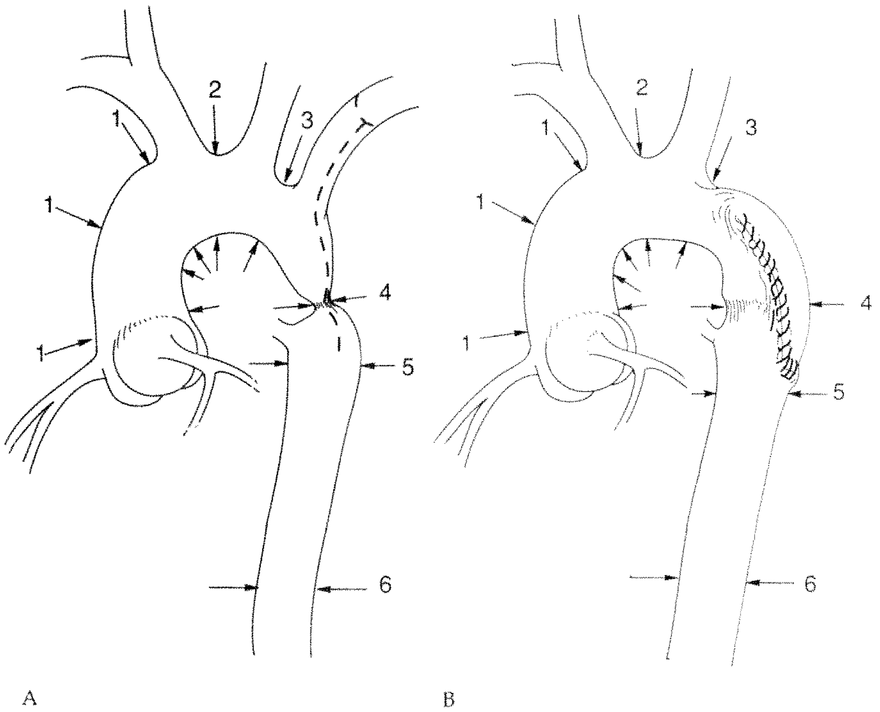


Fig 1. Diagram of aortogram preoperatively (A) and postoperatively (B). The numbers indicate the six regions where aortic diameters were measured.

or systemic to pulmonary artery shunt that could affect the differential growth of the aortic arch. They were used as age-matched controls.

The three measurements of the ascending aorta (proximal, mid, distal) were averaged, and the individual regions 2 through 6 were compared with region 1 and expressed as a percentage (region 2 percentage = region 2/region 1 × 100). Within each of these three groups, the mean value for each region was calculated and reported as mean ± standard error of the mean. The three groups were compared using analysis of variance; a p value less than 0.05 was considered significant.

The age at the time of each aortogram and the age at operation were recorded. Hemodynamic data to determine aortic pressure gradients were obtained from the most recent cardiac catheterization or two-dimensional Doppler echocardiographic studies, or both.

Results

Hemodynamic Data

The most recent cardiac catheterization or two-dimensional Doppler echocardiographic study was reviewed. In

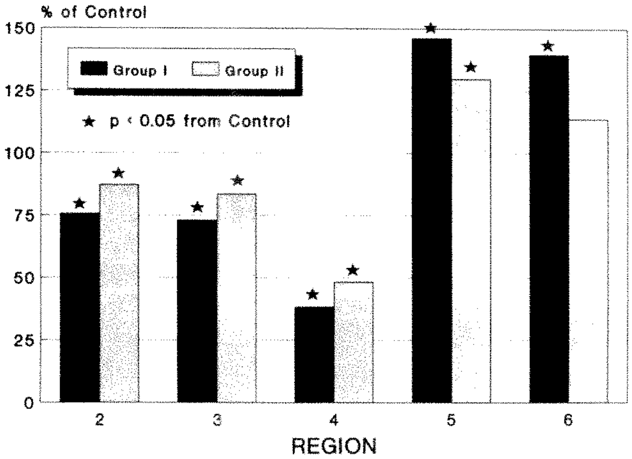


Fig 2. Preoperative aortic dimensional relationships: Aortic diameter relationship preoperatively at regions 2, 3, 4, 5, and 6 expressed as a percentage of the ascending aortic diameter.

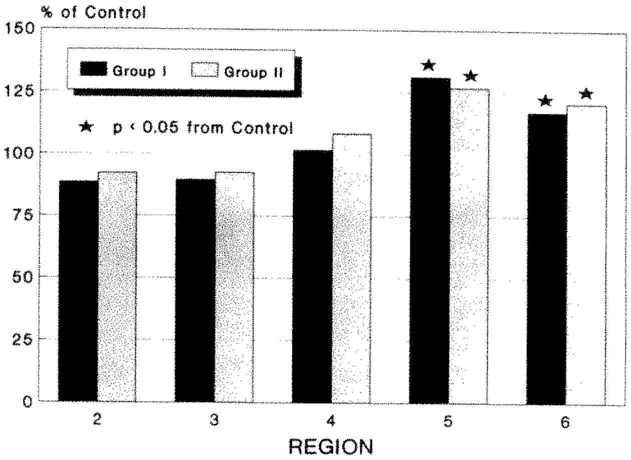


Fig 3. One-year postoperative follow-up aortic dimensional relationships: Aortic diameter relationship at 1 year postoperatively at regions 2, 3, 4, and 6 expressed as a percentage of the ascending aortic diameter.

Table 1. Preoperative Aortic Dimensional Relationships Based on Region 1 and Age at Surgical Intervention[a]

Region	Group I (<1 mo)	Group II (>1 mo)	Group III (controls <7 mo)	*p* Value (I vs III)	*p* Value (II vs III)	*p* Value (I vs II)
2	0.59 ± 0.10 (75.6%)	0.68 ± 0.04 (87.2%)	0.78 ± 0.06	<0.005	<0.005	
3	0.49 ± 0.06 (73.1%)	0.56 ± 0.05 (83.6%)	0.67 ± 0.05	<0.001	<0.002	<0.02
4	0.23 ± 0.08 (38.3%)	0.29 ± 0.11 (48.3%)	0.60 ± 0.07	<0.001	<0.001	
5	0.98 ± 0.11 (146.2%)	0.87 ± 0.15 (129.9%)	0.67 ± 0.06	<0.001	<0.02	
6	0.81 ± 0.11 (139.7%)	0.66 ± 0.08 (113.8%)	0.58 ± 0.03	<0.006		<0.006

[a] Number in parentheses is the percent of control.

groups I and II, no patient had a gradient of more than 10 mm Hg across the transverse aortic arch. One patient in group I had a 30 mm Hg gradient at the coarctation repair site secondary to a residual "ductal shelf." This patient subsequently underwent resection of the recurrent coarctation with no residual gradient.

Controls

Group III was divided into three categories: patients less than 8 months of age, patients 8 to 30 months of age, and patients more than 30 months of age at the time of the aortogram. There was no overall significant difference within the age categories in the control group (*F* test $p = 0.19$). There were differences, however, in some regions, particularly in the group less than 8 months old versus the group 30 months old and older. Therefore, comparisons between group III and groups I and II were made according to the age categories defined above. The diagnoses for these patients were restrictive ventricular septal defect (N = 4), Kawasaki's disease (N = 3), cardiomyopathy (N = 2), valvar pulmonary stenosis (N = 2), subaortic membrane without serious gradient (N = 2), posttraumatic mitral regurgitation (N = 1), and anomalous origin of the left coronary artery from the pulmonary artery (N = 1).

Preoperative Aortic Dimensions

In group I and group II, the regions of the aorta proximal to the coarctation (regions 2 and 3) site were all significantly smaller than control and the regions distal to the coarctation were significantly larger (Fig 2; Table 1). Regions 2, 3, and 4 were all smaller in group I than in group II, although statistical significance was only reached at region 3. The regions distal to the coarctation were larger in group I than in group II, although only region 6 was significantly different. Regions 5 and 6 in groups I and II were larger than in group III.

One-Year Postoperative Aortic Dimensions

One year after repair of the coarctation, the aortic arch (regions 2 and 3) and the coarctation site (region 4) had grown and were not significantly different from controls (Fig 3; Table 2). The regions distal to the coarctation repair site were still larger than controls.

Long-Term Postoperative Aortic Dimensions

The average age at long-term follow-up was 4.7 years (group I, 5.5 years; group II, 3.5 years). This follow-up showed that the aorta had continued to grow, although the aortic arch was smaller than controls at regions 2 and 3 in group II but only at region 2 in group I (Fig 4; Table 3). The regions distal to the coarctation repair site continued to be larger than controls.

Aortic Growth in Coarctation Repaired Before One Month of Age

Infants who underwent SFA at 1 month of age or younger were analyzed individually to determine the percent change in the aortic diameter, preoperatively and postoperatively, at each region of the aorta (Table 4). Growth occurred in the aortic arch (region 2, +13% ± 16%, and region 3, +23% ± 14%) and at the coarctation site (region 4, +57% ± 17%). This growth was statistically significant at regions 3 and 4. There was a statistically significant reduction in the postcoarctation dilatation at region 5 (−21% ± 14%) and region 6 (−14% ± 14%).

Aortic Growth in Coarctation Repaired After One Month of Age and Before One Year of Age

Infants who underwent SFA after 1 month of age but before they were a year old showed an increase in aortic

Table 2. One-Year Postoperative Follow-up Aortic Dimensional Relationships Based on Age at Surgical Intervention[a]

Region	Group I (<1 mo)	Group II (>1 mo)	Group III (controls <1 y)	*p* Value (I vs III)	*p* Value (II vs III)	*p* Value (I vs II)
2	0.69 ± 0.12 (88.5%)	0.72 ± 0.09 (92.3%)	0.78 ± 0.06			
3	0.60 ± 0.08 (89.6%)	0.62 ± 0.03 (92.5%)	0.67 ± 0.05			
4	0.61 ± 0.33 (101.7%)	0.65 ± 0.16 (108.3%)	0.60 ± 0.07			
5	0.88 ± 0.16 (131.3%)	0.85 ± 0.10 (126.9%)	0.67 ± 0.06	<0.02	<0.02	
6	0.68 ± 0.05 (117.2%)	0.70 ± 0.05 (120.7%)	0.58 ± 0.03	<0.003	<0.003	

[a] Number in parentheses is the percent of control.

Table 3. Long-Term Postoperative Follow-Up Aortic Dimensional Relationships Based on Age at Surgical Intervention[a]

Region	Group I (<1 mo)	Group II (>1 mo)	Group III (controls <1 y)	*p* Value (I vs III)	*p* Value (II vs III)	*p* Value (I vs II)
2	0.68 ± 0.06 (81.9%)	0.73 ± 0.04 (88.0%)	0.83 ± 0.06	<0.001	<0.001	
3	0.70 ± 0.07 (94.6%)	0.63 ± 0.05 (85.1%)	0.74 ± 0.05		<0.01	<0.01
4	0.63 ± 0.19 (90.0%)	0.80 ± 0.18 (114.3%)	0.70 ± 0.08			
5	0.79 ± 0.10 (112.9%)	0.85 ± 0.12 (121.4%)	0.70 ± 0.08	<0.04	<0.04	
6	0.71 ± 0.07 (114.5%)	0.70 ± 0.07 (112.9%)	0.62 ± 0.11	<0.02		

[a] Number in parentheses is the percent of control.

diameter at regions 2, 3, and 4 (+10% ± 6%, +12% ± 7%, and +65% ± 13%, respectively) (Table 5). There was no difference in the diameter of the aorta distal to the coarctation repair site.

Postoperative Aortic Growth in Infants

The growth of the aorta in individual patients was averaged for each group (Table 6). Comparing groups I and II, there was similar growth at regions 2 and 4. At region 3, there was more growth in group I. There was a greater reduction in postcoarctation dilation in group I at regions 5 and 6 (Fig 5).

Results Summary

Preoperatively, group I and group II had a smaller transverse aortic arch (regions 2 and 3) than the control group. Postoperative diameters of the transverse aortic arch obtained 1 year later were also similar in groups I and II, although there was less growth of the transverse arch in groups I and II when compared with group III. When comparing the postoperative arch diameter with the preoperative transverse aortic arch diameter in each patient, there was a significant increase in group I as compared with group II (23% ± 14% and 12% ± 7%, respectively; $p < 0.03$).

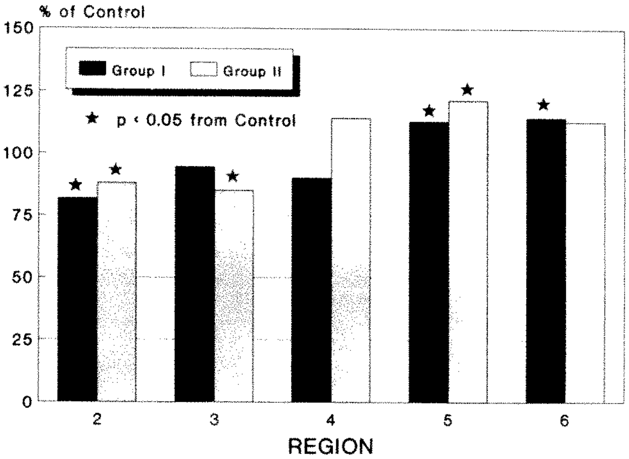


Fig 4. Long-term postoperative follow-up aortic dimensional relationships: Aortic diameter relationship long-term postoperatively at regions 2, 3, 4, 5, and 6 expressed as a percentage of the ascending aortic diameter.

Comment

The hemodynamic molding theory proposes that blood vessels grow around a column of flowing blood. Coarctation and isthmus hypoplasia are thought to be the result of a disturbance in fetal blood flow that increases pulmonary artery flow and decreases aortic flow [13, 14]. The most severe reduction in left heart output causes hypoplastic left heart syndrome, in which the ascending aorta is severely hypoplastic and carries blood flow retrograde only to the coronary arteries. Lesser reductions in left heart output results in interrupted aortic arch, hypoplastic aortic arch, and coarctation of the aorta.

If the coarctation is repaired early, one might expect hemodynamic molding to occur, enabling the aortic arch to develop to normal dimensions. It is not known for how long after birth this hemodynamic molding concept may be functional. In our clinical experience with 2 patients who underwent repair of coarctation after 1 year of age (SFA in 1 patient and end-to-end anastomosis in the other) subsequent catheterization demonstrated aortic arch gradients of 40 mm Hg or more proximal to the coarctation repair site in a small transverse aortic arch. An ascending aorta to descending aorta tube graft was placed to abolish the gradient. In contrast, the results of the present study and the report by Siewers and associates [15] show that a moderately hypoplastic aortic arch does grow when the coarctation is repaired in early infancy.

The extended aortic arch anastomosis in repair of coarctation of the aorta is performed by incising the inferior aspect of the aortic isthmus and arch (usually just proximal to the origin of the left carotid artery) and anastomosing it to the obliquely trimmed descending aorta [7–10]. Although this and the SFA techniques effectively eliminate the coarctation and augment the aortic isthmus and

Table 4. Aortic Growth in Patients Less Than One Month of Age at Time of Surgical Intervention (Group I)

Region	Preoperative	Postoperative	% Change	*p* Value (pre vs post)
2	0.59 ± 0.10	0.68 ± 0.07	+13 ± 16	0.05
3	0.49 ± 0.06	0.67 ± 0.09	+23 ± 14	<0.001
4	0.23 ± 0.08	0.65 ± 0.24	+57 ± 17	<0.001
5	0.98 ± 0.11	0.82 ± 0.13	−21 ± 14	<0.02
6	0.81 ± 0.11	0.70 ± 0.06	−14 ± 14	<0.02

Table 5. Aortic Growth in Patients More Than One Month of Age at Time of Surgical Intervention (Group II)

Region	Preoperative	Postoperative	% Change	*p* Value (pre vs post)
2	0.68 ± 0.04	0.74 ± 0.05	+10 ± 6	<0.03
3	0.56 ± 0.05	0.63 ± 0.05	+12 ± 7	<0.03
4	0.29 ± 0.11	0.81 ± 0.19	+65 ± 13	<0.011
5	0.87 ± 0.15	0.82 ± 0.12	−3 ± 10	
6	0.66 ± 0.08	0.67 ± 0.06	+4 ± 10	

the aortic arch between the left carotid and left subclavian arteries, they do not usually enlarge that portion of the aortic arch between the innominate and left carotid arteries. In our experience with these techniques, resting gradients are rarely observed and the repair is considered successful. The narrowest point of the aortic arch is, however, frequently between the innominate and left subclavian arteries just proximal to the proximal aspect of the repair. Thus, growth of this area is important for a good long-term result in patients after either operation.

Postnatally, the growth potential of the aorta due to hemodynamic molding tends to diminish gradually. Infants less than 1 month of age showed greater growth potential than infants who were older than 1 month at the time of repair. At region 3, just proximal to the coarctation repair site, group I infants showed a 23% increase in luminal diameter, whereas group II infants had only a 12% increase in luminal diameter when compared with control.

The operative mortality for extended end-to-end aortic arch anastomosis ranges from 6% to 26% with a restenosis rate of around 12% [7–10, 16]. The operative mortality for SFA has been 4% to 12% in most series [3–6, 17]. The restenosis rate ranges from 3% to 25% in most series [3–6, 17]. The operative mortality for SFA tends to be lower than that reported for extended end-to-end aortic arch anastomosis and the restenosis rate is similar. There is considerable overlap in the data, and statistically there is probably no difference in operative mortality or restenosis.

A precise definition of hypoplastic aortic arch is difficult. The exact size for what is hypoplastic and what is small is very difficult because it is dependent on the age, weight, and gestation of the infant. Most infants with coarctation have an aortic arch that is smaller than normal, as we have shown (see Table 1). It is this spectrum of coarctation that is addressed in this report. Although these small aortic arches are not severely "hypoplastic" it is still necessary for these aortic arches to grow so that a gradient will not develop as the patient grows to adulthood.

Table 6. Comparison of Aortic Growth Between Group I and Group II (Percent Change)

Region	Group I (<1 mo)	Group II (>1 mo)	*p* Value (I vs II)
2	+13 ± 16	+10 ± 6	
3	+23 ± 14	+12 ± 7	<0.03
4	+57 ± 17	+65 ± 13	
5	−21 ± 14	−3 ± 10	<0.003
6	−14 ± 14	+4 ± 10	<0.003

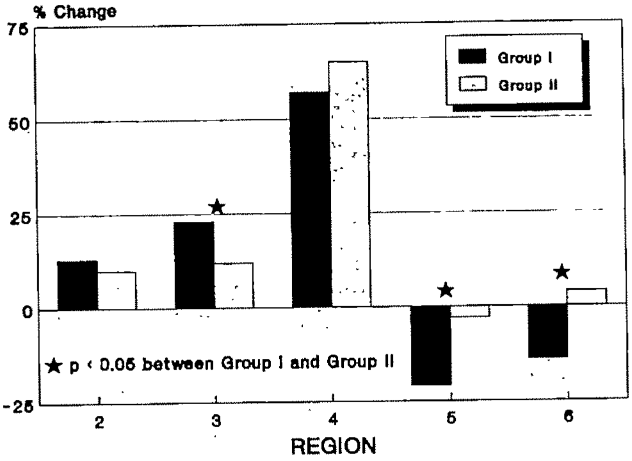


Fig 5. Aortic growth from preoperative to postoperative: The percent change in aortic diameter from preoperative to postoperative aortograms in individual patients in group I and group II.

Clearly, there are some patients who have serious tubular hypoplasia of the aortic arch that extends proximal to the left subclavian artery, and if they had only repair of the coarctation of the aorta, they would still have a hypoplastic aortic arch segment with a substantial residual obstruction. In our institution, these patients are managed by the extended aortic arch anastomoses; more difficult cases require a median sternotomy approach using deep hypothermia and circulatory arrest and extensive arch augmentation or primary anastomosis similar to repair of interrupted aortic arch.

The infants in this study were all believed to have an aortic arch that was small but large enough to support postoperative flow without a serious gradient. In 2 infants who are not in this series because they did not have aortograms preoperatively and postoperatively, the aortic arch was small and after SFA, a gradient remained across the aortic arch. Both infants were symptomatic and required augmentation of the aortic arch by 3 months after operation.

At the two extremes, the severely hypoplastic transverse aortic arch at the one end and the normal arch with discrete coarctation at the other, the decision as to which operation is best is easy to make. This study has shown that the small aortic arch can grow. Therefore, the patient with a normal or small aortic arch should have a simple repair. However, there may be a few small arches that fail to grow. This may be secondary to abnormal aortic tissue in the aortic arch. Unfortunately, these patients will require a second operation to enlarge the aortic arch. We have not been able to predict this lack of growth in our experience.

The age at which elective surgical repair of a coarctation is done must be chosen to avoid both recoarctation at one side or the development of chronic hypertension at the other. Because at the age of 3 years the cross-sectional area of the thoracic aorta is 75% of that of an adult, restenosis is uncommon in patients operated on after this age, even when resection and end-to-end anastomosis is used [18]. This must be balanced with the potential side effects of prolonged preoperative hypertension and other vascular changes. The earlier the age at operation, the greater the likelihood of normal postoperative blood pressure [5, 6]. Elective coarctation repair, therefore, is recommended at even younger ages as surgical results, both immediate and long-term, improve. Thus, elective repair at 12 months is now recommended by us and by others rather than waiting until the more traditional age of 4 years [4]. Our study shows that after very early correction by the subclavian flap procedure, growth potential at the coarctation site and at the proximal smaller regions of the aortic arch increases. These findings support the decision to operate and repair aortic coarctation earlier rather than later. Infants less than 1 month of age exhibit greater growth potential of the aortic arch, making the risk of residual aortic arch "stenosis" even less.

In conclusion, growth of the small transverse aortic arch does occur after SFA. This growth is more pronounced in infants who had the coarctation repaired before 1 month of age. These findings add further to the concept of early repair. Furthermore, the results suggest that radical repairs of coarctation of the aorta with transverse aortic arch enlargement usually required for the hypoplastic aortic arch are not necessary in patients with a small aortic arch if coarctation of the aorta itself is adequately repaired.

References

1. Williams WG, Shindo G, Trusler GA, Dische MR, Olley PM. Results of repair of coarctation of the aorta during infancy. J Thorac Cardiovasc Surg 1980;79:603–8.
2. Harlan JL, Doty DB, Berkeley B, Ehrenhaft JL. Coarctation of the aorta in infants. J Thorac Cardiovasc Surg 1984;88:1012–9.
3. Ziemer G, Jonas RA, Perry SB, Freed MD, Castaneda AR. Surgery for coarctation of the aorta in the neonate. Circulation 1986;74(Suppl 1):25–31.
4. Campbell DB, Waldhausen JA, Pierce WS, Fripp R, Whitman V. Should elective repair of coarctation of the aorta be done in infancy? J Thorac Cardiovasc Surg 1984;88:929–38.
5. Kopf GS, Hellenbrand W, Kleinman C, Lister G, Talner N, Laks H. Repair of aortic coarctation in the first three months of life: immediate and long-term results. Ann Thorac Surg 1986;41:425–30.
6. Penkoske PAS, Williams WG, Olley PM, et al. Subclavian arterioplasty: repair of coarctation of the aorta in the first year of life. J Thorac Cardiovasc Surg 1984;87:894–900.
7. Vouhé RE, Trinquet F, Lecompte Y, et al. Aortic coarctation with hypoplastic aortic arch: results of extended end-to-end aortic arch anastomosis. J Thorac Cardiovasc Surg 1988;96:557–63.
8. Lacour-Gayet F, Bruniaux J, Serraf A, et al. Hypoplastic transverse arch and coarctation in neonates. J Thorac Cardiovasc Surg 1990;100:808–16.
9. Zannini L, Lecompte Y, Galli R, et al. Aortic coarctation with hypoplasia of the arch: description of a new surgical technique. G Ital Cardiol 1985;15:1045–8.
10. Amato JJ, Rheinlander HF, Cleveland RJ. A method of enlarging the distal transverse arch in infants with hypoplasia and coarctation of the aorta. Ann Thorac Surg 1977;23:261–3.
11. Pae WE, Myers JL, Waldhausen JA, Prophet GA, Pierce WS. Subclavian flap angioplasty. J Thorac Cardiovasc Surg 1981;82:922–7.
12. Waldhausen JA, Nahrwold DL. Repair of coarctation of the aorta with a subclavian flap. J Thorac Cardiovasc Surg 1966;51:532–3.
13. Rudolph AM, Heymann MA, Spitznas U. Hemodynamic considerations in the development of narrowing of the aorta. Am J Cardiol 1972;30:514–25.
14. Shinebourne EA, Elseed AM. Relation between fetal flow patterns, coarctation of the aorta, and pulmonary blood flow. Br Heart J 1974;36:492–8.
15. Siewers RD, Ettedgui J, Pahl E, Tallman T, del Nido PJ. Coarctation and hypoplasia of the aortic arch: will the arch grow? Ann Thorac Surg 1991;52:608–14.
16. Lansman S, Shapiro AJ, Myles S, et al. Extended aortic arch anastomosis for repair of coarctation in infancy. Circulation 1986;74:37–41.
17. Metzdorff MT, Cobanoglu A, Grunkemeier GL, Sunderland CO, Starr A. Influence of age at operation on late results with subclavian flap aortoplasty. J Thorac Cardiovasc Surg 1985;89:235–41.
18. Beekman RH, Rocchini AP, Behrendt DM, Rosenthal A. Reoperation for coarctation of the aorta. Am J Cardiol 1981;48:1108–14.

DISCUSSION

MR JAROSLAV F. STARK (London, England): Dr Myers, were any of the ten neonatal aortic arches actually hypoplastic? If so, how do you define it? The third part of the aortic arch is usually smaller in neonates but only in 20% to 25% of neonates with coarctation of the aorta it is truly hypoplastic. I think this is a very important point as you have concluded that extended repair is not necessary.

In our department we are currently reviewing the data on 151 infants with coarctation of the aorta operated on during the first 3 months of life. We have used subclavian flap, resection, extended resection, and radically extended resection. There was no difference in mortality between the four techniques. However, survival free of recoarctation was much better (96%; confidence limits, 77% to 100%) after radically extended resection compared with the other three techniques.

DR MYERS: First let me say that we know coarctation has a very wide spectrum. We have had patients who have had an extended repair where the descending aorta is brought up underneath the ascending aorta because we believed that those areas in the transverse aortic arch between the innominate and left carotid arteries or left carotid and left subclavian arteries would still be too small and have a serious gradient in the early postoperative period if a subclavian flap angioplasty was performed.

In a few patients in whom we believed that the hypoplasia was severe we have done an interrupted arch type repair with deep hypothermic circulatory arrest from a median sternotomy approach. In these patients, the transverse aortic arch has been on the order of 1 to 2 mm, and we have not thought that those patients were candidates for just an isolated coarctation repair.

What led us to this study was that we had a patient several years ago who was actually older than 1 year of age and had a subclavian flap angioplasty. In subsequent follow-up she had evidence of narrowing in the transverse aortic arch, and it was clear that there was no residual coarctation, but that the area in the transverse aortic arch was small. We therefore wanted to look back at our coarctation group that had been repaired earlier in life and find out if the transverse aortic arch growth kept up with what we would consider normal growth.

MR STARK: I think you have shown that the small aortic arch will grow; but the question is will the truly hypoplastic aortic arch grow? From what you said I believe that there were no patients with truly hypoplastic arch in the group you have studied.

DR MYERS: I think we would consider these patients to have moderately hypoplastic or small aortic arches. They were not the 1-mm or 2-mm aorta.

MR STARK: A 3-mm aortic arch in a 2-kg baby may still be normal.

DR MYERS: The arches that we observed had very severe tapering beyond the innominate artery.

DR JOHN W. HAMMON, JR (Winston-Salem, NC): I think it all gets down to the question that is being debated mostly in pediatric cardiac surgical circles: What are the exact indications for subclavian flap angioplasty and for radical arch repair? I think that question has yet to be answered, and perhaps more discussions like this will help clarify the issues.

DR C. E. ANAGNOSTOPOULOS (New York, NY): Parallel growth of rectus sheath and aorta in experimental preparations has been observed, and it is very close to that of the aorta. Recently we confirmed this in 7 patients who had a variety of patches. Have you had in these patients (other than the 17 that you studied) situations where the arch failed to grow because of persistent obstruction, inadequate repair, or any other number of reasons? Also, have you considered other tissue augmentation to the Waldhausen flap angioplasty?

DR MYERS: To answer the second question first, no, we have not used any other autologous tissue. We have just used the subclavian flap. We have used it not only flap-based proximally, as the standard subclavian flap angioplasty, but in some patients where there has been some discrete hypoplasia more proximally the flap has been swung proximally.

We have many other patients who had subclavian flap angioplasty who were not included in this study because they did not have both preoperative and postoperative studies. Two patients had serious gradients postoperatively in the aortic arch and required patch augmentation of transverse aortic arch. We have had some patients older than a year of age who have had subclavian flap angioplasty; 2 patients have required an ascending aorta to descending aortic graft because of persistent gradients in the transverse aortic arch.

DR HILLEL LAKS (Los Angeles, CA): I would like to make a practical suggestion about this issue of the hypoplastic segment between the carotid and left subclavian arteries. The ones that we worry about are those in which that segment has a diameter less than 50% of the diameter of the aorta at the level of the diaphragm, and in those cases, if they are borderline, we would do the subclavian flap aortoplasty and then measure gradient. If there is a gradient greater than 30 or 40 mm Hg, we have in 2 patients used the carotid artery as a second aortoplasty flap, extending the incision down the carotid, across that segment of arch between carotid and subclavian, and onto the subclavian flap itself, so that the carotid then acts as a flap enlarging that segment of the arch as well as the proximal part of the subclavian flap.

I do not know if you have had any experience with that approach.

DR MYERS: We have had experience with using the carotid as a flap as you describe. We have also used the carotid and the subclavian and incised them each longitudally and then anastomosed them together in a spatulated fashion so that the subclavian is positioned proximally and the carotid artery is positioned distally so that they are overlapping to create a large tubular reconstruction.

DR JOSEPH J. AMATO (New Hyde Park, NY): Dr Myers, there are three separate points to be made here. I believe the point you are stressing is that a small aortic arch can and does grow, which many of us concur with. The second point is that undoubtedly in most repairs end-to-end anastomosis or subclavian flap is ideal, which again many would agree with. But you are also as a third point saying, as Mr Stark pointed out, that where you truly have a hypoplastic situation, you do use other procedures for augmentation. I just want to clarify that point.

DR MYERS: Yes.

DR AMATO: I believe that some in the audience might be thinking that we should never augment or we should never extend the resection to include the arch.

DR MYERS: No, I do not mean to imply that. In those areas of the transverse aortic arch that we feel are very hypoplastic, we have used the extended end-to-end anastomosis and we have also repaired some patients as an interrupted arch.

Postinfarct Ventricular Septal Defect Repair: Effect of Coronary Artery Bypass Grafting

Derek D. Muehrcke, MD, Willard M. Daggett, Jr, MD, Mortimer J. Buckley, MD,
Cary W. Akins, MD, Alan D. Hilgenberg, MD, and W. Gerald Austen, MD

Surgical Cardiovascular Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Between June 1968 and April 1991, 75 patients who had undergone coronary angiography underwent repair of a postinfarction ventricular septal defect. Group 1 (n = 33) includes patients who had two- or three-vessel serious (>75% narrowing) proximal coronary artery disease and underwent complete revascularization in addition to repair of the ventricular septal defect. Group 2 (n = 19) patients also had two- or three-vessel coronary artery disease but bypass grafting was not performed; only the ventricular defect was repaired. Group 3 (n = 23) patients had only single-vessel coronary artery disease that corresponded to the region of the infarct; they underwent ventricular septal defect repair only. Follow-up of hospital survivors was 96% complete at a mean of 86.2 months (range, 1 to 288 months). Hospital mortality after ventricular septal defect repair was 21.2% in the cohort with bypassed coronary artery disease (group 1), 26.3% in those with unbypassed disease (group 2), and 26.1% in those with only single-vessel coronary artery disease (group 3) ($p = 0.88$). With follow-up after 5 and 10 years, the actuarial survival was 72.2% ± 8% and 47.8% ± 10%, respectively, in the bypassed group, 29.2% ± 11% and 0%, respectively, in the unbypassed group, and 52.2% ± 10% and 36.5% ± 11%, respectively, in the cohort with single-vessel disease. Bypassing associated coronary artery disease significantly increased long-term survival when compared with patients with unbypassed coronary artery disease ($p = 0.0015$).

(Ann Thorac Surg 1992;54:876–83)

Ventricular septal defect (VSD) is an infrequent yet serious complication of acute myocardial infarction. Untreated patients have a 24% mortality within the first day and an 80% mortality within the first month [1]. With surgical treatment, however, patients have an opportunity for improved survival. Current surgical mortality rates range from 10% to 40% [2–6], with as many as 88% of the operative survivors alive after 5 years [7]. Despite numerous improvements in the surgical techniques used to repair this usually fatal lesion, the effect of bypassing hemodynamically significant coronary atherosclerosis coincident with VSD repair is not known. Although frequently performed, bypass grafting of diseased vessels at the time of VSD repair has been condemned by some surgeons despite the etiologic role of coronary artery disease (CAD) in the development of septal rupture [8, 9].

Some authors have suggested that long-term surgical mortality after VSD repair relates more to factors other than revascularization and that the time spent performing (and the dye load pursuant to) coronary angiography may be dangerous. Mattila and associates [10], for example, have suggested that the contractility of the noninfarcted left ventricle will improve after simple repair of the defect and excision of any aneurysm segment without bypass grafting. They argue that septal repair decreases left ventricular wall tension and myocardial oxygen consumption, obviating the need for revascularization. Other investigators have stated that concomitant revascularization provides no early survival benefit and subjects patients to time-consuming and potentially dangerous diagnostic studies [8, 9]. Nonetheless, many surgeons continue to obtain coronary angiograms in all patients with postinfarction ventricular septal rupture and to perform coronary artery bypass grafting (CABG) where indicated [2–4, 6, 11]. We therefore reviewed our experiences to investigate the early and late effects of coronary artery revascularization in patients undergoing repair of a postinfarction VSD.

Material and Methods

Between June 1968 and April 1991, 86 patients underwent repair of a postinfarction VSD at the Massachusetts General Hospital. Eleven patients did not have coronary angiography performed, and because their coronary artery anatomy was unknown they were excluded from this study. The remaining 75 patients underwent coronary artery angiography before operation and form the basis of this report. The charts of these latter patients were retrospectively reviewed and analyzed. For purposes of comparing the effects of coronary artery revascularization, patients were divided into three groups. Group 1 (n = 33) includes patients who had two- or three-vessel, serious, proximal CAD, with one or two involved vessels outside the area of the VSD; these patients underwent complete revascularization in addition to repair of the VSD. Group 2 (n = 19) patients also had one or two vessels with CAD

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Daggett, Department of Surgery, Massachusetts General Hospital, Boston, MA 02114.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

in addition to the occluded vessel that caused the ventricular defect. In this group, however, bypass grafting was not performed despite the associated coronary vascular disease; these patients only had the VSD repaired. Group 3 (n = 23) patients had only single-vessel CAD that corresponded to the region of infarcted ventricular septum. These patients underwent repair of the septal defect only. Coronary angiography reports in the medical record were used to determine the extent of CAD. All stenoses were proximally located in the vessels and had a greater than 75% luminal narrowing (50% decrease in diameter).

Table 1 presents data on all three groups of patients. The mean ages for all groups were similar. Patients greater than 65 years of age were evenly distributed among the three groups. Male patients were operated on more frequently than female patients in all three groups. In group 1 there were 87 diseased coronary vessels in 33 patients; 12 patients had double-vessel disease, and 21 patients had triple-vessel disease. In group 2, 49 diseased vessels were identified in 19 patients; 8 patients had double-vessel disease and 11 patients had triple-vessel CAD. All patients in group 3 had single-vessel CAD involving the area of the infarct. Patients in group 1 underwent CABG ×1 in 12 patients, CABG ×2 in 17 patients, CABG ×3 in 3 patients, and CABG ×4 with a left internal mammary artery anastomosis to the left anterior descending artery in 1 patient. Anterior (including apical defects) and posterior septal ruptures were equally distributed in groups 1 and 2. However, patients in group 3 with less severe coronary artery disease had more anterior defects.

Table 1. Patient Data, Distribution of Coronary Artery Disease, and Location of Septal Defects[a]

Variable	Group 1 (bypassed 2- or 3-vessel disease)	Group 2 (unbypassed 2- or 3-vessel disease)	Group 3 (single-vessel disease)
No. of patients	33	19	23
Mean age (y)	65.8 ± 8.3	65.4 ± 5.9	63.9 ± 7.9
No. of patients aged >65 y	16 (45.1%)	9 (47.3%)	9 (39%)
Sex			
Male	19 (57.6%)	11 (57.9%)	12 (52.2%)
Female	14	8	11
No. of coronary arteries narrowed	87 in 33 pts	49 in 19 pts	23 in 23 pts
2	12 (36.4%)	8 (42.1%)	0
3	21 (63.6%)	11 (57.8%)	0
CABG procedures			
1	12		
2	17		
3	3		
LIMA/CABG × 4	1		

[a] Data expressed as mean ± standard error of the mean.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; LIMA = left internal mammary artery; pts = patients; VSD = ventricular septal defect.

Table 2. Preoperative Patient Data[a]

Variable	Group 1 (bypassed 2- or 3-vessel disease)	Group 2 (unbypassed 2- or 3-vessel disease)	Group 3 (single-vessel disease)
No. of patients	33	19	23
Shock	11 (33%)	6 (31.6%)	10 (43.5%)
IABP	23 (69.7%)	11 (57.9%)	15 (65.2%)
Catecholamines	30 (91%)	16 (84.2%)	17 (73.9%)
Aortic systolic pressure (mm Hg)	97.2 ± 15	87.17 ± 20	98.3 ± 15
PCWP (mm Hg)	18.97 ± 4.8	21.6 ± 5.8	18.4 ± 4.2
RAP (mm Hg)	9.6 ± 4.6	11.1 ± 7.0	10.1 ± 4.1
Qp/Qs	3.52 ± 1.09	3.54 ± .73	3.24 ± 1.7
BUN	33.26 ± 11.9	33.36 ± 18.4	32.6 ± 12.7
Mean days to operation	19.97 ± 24	20.39 ± 24.6	28.6 ± 24

[a] Data expressed as mean ± standard error of the mean.

BUN = blood urea nitrogen level; IABP = intraaortic balloon pump; PCWP = pulmonary capillary wedge pressure; Qp/Qs = pulmonary to systemic shunt ratio; RAP = right atrial pressure.

Table 2 presents hemodynamic data measured preoperatively for all three groups: aortic systolic pressure, pulmonary capillary wedge pressure, right atrial pressure, left-to-right shunt as calculated by applying the Fick equation to both the pulmonary and systemic circuits and subtracting the systemic flow from the pulmonary blood flow [12], preoperative blood urea nitrogen level, and number of days to operation after onset of infarction. All recorded pressures were the last preoperative values available. Cardiogenic shock was defined as sustained arterial hypotension (systemic arterial pressure less than or equal to 85 mm Hg) accompanied by oliguria (urine output less than 20 mL/h for 4 or more hours). Patients with isolated systolic arterial hypotension associated with chronic low cardiac output or congestive heart failure, unaccompanied by oliguria, were not categorized as in shock. Eleven patients in group 1, 6 in group 2, and 10 in group 3 manifested cardiogenic shock preoperatively. Intraaortic balloon counterpulsation, as well as preoperative or postoperative catecholamine support, was used frequently and equally in all groups.

In each patient the presence of a VSD was diagnosed by detecting an increase in blood oxygen saturation when comparing blood in the right atrium with blood in the pulmonary artery. All patients demonstrating this type of oxygen "step-up" were found to have a septal defect at the time of operation. The anatomic location of the defect in the ventricular septum, confirmed at operation, correlated with the distribution of the infarct as indicated by the preoperative electrocardiogram in all but 4 patients. In each of these 4 patients the left anterior descending artery wrapped around the apex of the left ventricle to supply the distal aspect of the posterior septum. Although the electrocardiogram suggested an inferior infarction, the septal defect was positioned at the apex of the heart. Two patients in group 2 underwent concurrent mitral valve replacement for a ruptured papillary muscle, and 1 patient in group 3 similarly underwent mitral valve replacement. As only 1 of these patients in group 2 died early postoperatively this was not believed to be a confounding variable, and these patients were included in the analysis.

Surgical Technique

With hemodynamic monitoring by central venous, radial, and pulmonary artery catheters, general endotracheal anesthesia was induced. After median sternotomy, systemic heparinization, and cannulation, cardiopulmonary bypass was accomplished with a bubble (or more recently with a hollow fiber membrane) oxygenator. Before 1977, hypothermic fibrillatory arrest at 28°C was used, and after 1977 myocardial protection consisted of systemic hypothermia (20° to 25°C) with intermittent multidose cold potassium cardioplegia infused into the aortic root. Thirty-six patients were operated on before and 39 after 1977. Coronary artery bypass grafting was performed using reverse saphenous vein with the proximal anastomoses performed first. One internal mammary artery graft was used in a patient with three-vessel disease. Infarctectomy or aneurysmectomy was performed when appropriate [2, 13, 14].

For a review of our operative techniques see the articles by Daggett and associates [2, 13–15]. Apical ventricular septal defects secondary to anterior myocardial infarction were repaired using the technique of apical amputation [15]. High anterior defects were repaired through a transinfarct incision made in the left ventricle parallel to the left anterior descending artery. When there was little loss of septal tissue, primary repair was performed with felt-buttressed interrupted sutures. To avoid tension on the repair, larger septal defects were closed using an elasticized Dacron patch. Posteriorly located defects were more difficult to repair and were approached through the area of infarct in the posterior left ventricle [13, 14]. All infarcted muscle was resected back to viable tissue based on gross appearance to ensure that the sutures would not rupture. Large ventricular defects were closed with an elasticized Dacron patch, whereas smaller defects were closed by approximating the edge of the septum to the free wall of the right ventricle using felt-buttressed mattress sutures. In group 1, 24 patients (72%) required a Dacron patch to close the VSD; 13 patients in group 2 (68%) required a patch. However, only 8 patients (34.8%) in group 3 required patches to close the ventricular defect. Patch closure of the defect was generally used when the defect was large and there was concern that tension at the repair site might cause a simple closure to fail. The remaining posterior infarctectomy defect in the left ventricular free wall was closed with a patch of low-porosity woven Dacron to prevent excessive tension on the closure as previously described [2, 14].

Bypass grafting was not performed on patients in group 2 due to either the operating surgeon's judgement not to perform bypass grafting or inadequate or absent conduit (eg, prior vein stripping or varicose veins). Only 5 patients out of a total of 75 patients with known coronary anatomy (6.6%) were thought to have inadequate or unavailable conduit due to prior saphenous vein stripping. Initially emphasis was placed on dealing with the immediate, life-threatening problem of the acute septal defect and correction of the left to right shunt. However, as experience was gained with the techniques of VSD repair and the level of confidence in closure methods increased, it was thought that concomitant CABG could be safely performed at the time that the septal defect was repaired. Thus more patients had CABG later in the series.

Statistical Analysis

Statistical analyses were conducted in SAS-PC (SAS Institute Inc, Cary, NC). Continuous variables are expressed as the mean ± the standard error of the mean. Comparisons between continuous variables for the three groups were made with one-way analysis of variance followed by Duncan's multiple-range test if the p value was less than 0.05 [16]. Discrete variables were compared by means of χ^2 analysis or by Fisher's exact test [17]. Survival curves were constructed using the life-table actuarial method, and all operative deaths were included in the analysis [18]. Differences in survival curves were assessed with the generalized Wilcoxon test. For all univariate analysis, the α level was set at 0.05.

Postoperative follow-up information was obtained from hospital chart review, telephone interview of the patient or referring physician, and review of office charts. Follow-up of hospital survivors ranged from 1 to 288 months (mean, 86.2 months) and was compiled in April and May 1991. Three patients were lost to follow-up (4%). Postoperative data included status at follow-up (alive, dead, lost to follow-up), cause of death, and New York Heart Association functional class. Early mortality was defined as death during the initial hospitalization or within 30 days of operation. Causes of death were classified into four groups on the basis of clinical and pathological findings. Cardiac-related causes included congestive heart failure and myocardial infarction. Noncardiac causes of death included death due to technical problems (intraoperative deaths due to tearing out of sutures or recurrence of VSD in the acute postoperative period), sepsis, or cerebral vascular accident. Long-term deaths (>30 days postoperatively or after discharge) were classified as cardiac (recurrence of septal defect postoperatively, congestive heart failure, myocardial infarction), cerebral vascular accidents, cancer, or sepsis (eg, pneumonia).

Results

The distribution of preoperative and postoperative variables by cohort is shown in Tables 1 and 2. Comparison of the patients with bypassed and unbypassed multivessel CAD and those with single-vessel CAD demonstrated that the three cohorts were similar in terms of mean age, number of patients greater than age 65 years, sex, shock, use of intraaortic balloon pump, and use of catechola-

Table 3. Degree of Coronary Artery Disease by Location of Ventricular Septal Defects[a]

Location of VSD	Single-Vessel Disease	2- or 3-Vessel Disease
Anterior	15 (65.2%)	19 (36.5%)
Posterior	8 (34.7%)	33 (63.5%)

[a] Data expressed as mean ± standard error of the mean.

VSD = ventricular septal defect.

mines. Other preoperative comparative data were similar in all three groups, including aortic systolic pressures, pulmonary capillary wedge pressures, right atrial pressure, shunt ratio, preoperative blood urea nitrogen level, and days between infarction and operation.

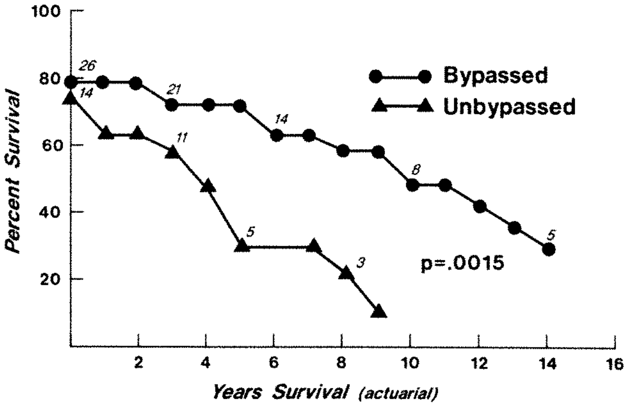


Fig 1. Long-term survival of bypassed (group 1) versus nonbypassed patients (group 2). Operative deaths are included in determinations. The patients undergoing coronary artery bypass grafting in addition to ventricular septal defect repair lived longer than those patients with unbypassed coronary artery disease.

Table 4. Follow-up Data on Survival and Mortality

Variable	Group 1 (bypassed 2- or 3-vessel disease)	Group 2 (unbypassed 2- or 3-vessel disease)	Group 3 (single-vessel disease)
Hospital survivors	26 (78.8%)	14 (73.6%)	17 (73.9%)
Causes of hospital deaths	7	5	6
Cardiac	2 (28.5%)	3 (60%)	2 (33.3%)
Technical	2	1 (20%)	0
Sepsis	2	1	4 (66.6%)
CVA	1 (14.3%)	0	0
Follow-up			
Percent complete	93.9%	94.7%	100%
Average length (mo)	93.4	61.9	95.3
Range (mo)	1–288	12–115	1–194
Causes of long-term deaths	9	11	11
Cardiac	4 (44.4%)	6 (54.5%)	3 (27.3%)
Sepsis	1 (11%)	1 (9%)	1 (9%)
CVA	2 (22%)	2 (18%)	3
Cancer	2	2	3

CVA = cerebral vascular accident.

The patients with single-vessel disease needed fewer patch closures to repair their septal defects, indicating they had smaller defects ($p = 0.012$). There was also a statistically significant difference in the distribution of CAD among the three patient groups (Table 3). Those patients with only single-vessel coronary artery disease had more anteriorly located septal defects as opposed to those patients with two- or three-vessel coronary disease, who had a much higher incidence of posteriorly located septal defects ($p = 0.015$). The cumulative 30-day mortality after VSD repair was 21.2% in the cohort with bypassed CAD, 26.3% in those with unbypassed disease, and 26.1% in those with only single-vessel CAD ($p = 0.88$) (Table 4). There was a trend, though of borderline statistical significance ($p = 0.055$), toward a greater number of patients with single-vessel disease being operated on earlier in our experience (before 1975), when we were developing our surgical technique and when the operative mortality rate was greater in all patients for technical reasons [2]. The increased operative mortality rate before 1975 may have influenced the overall mortality rate in the group of patients with single-vessel disease.

If a more even distribution of patients with single-vessel disease had been operated on during the entire period reviewed from 1968 to 1991, perhaps the patients with single-vessel disease would have demonstrated an improved hospital survival and long-term survival relative to all groups. Table 3 lists the causes of hospital deaths, long-term follow-up data, and causes of long-term deaths. Bypassing associated CAD significantly increased long-term survival when compared with patients with unbypassed CAD ($p = 0.0015$). The enhanced survival of the bypassed patients persisted during the follow-up period in actuarial survival analysis (Fig 1). With follow-up after 5 and 10 years, survival was 72.2% ± 8% and 47.8% ± 10%, respectively, in the bypassed group, 29.2% ± 11% and 0%, respectively, in the unbypassed group, and 52.2% ± 10% and 36.5% ± 11%, respectively, in the cohort with single-vessel disease (Fig 2).

Each group studied (men, women, posterior VSDs, anterior VSDs, those having bypass before or after the introduction of cardioplegia) benefited from bypassing associated CAD when compared with their unbypassed cohort. There was no difference, however, in the long-term survival at 10 and 15 years between the bypassed group and the group with single-vessel coronary artery disease ($p = 0.53$). The group with single-vessel disease lived significantly longer than the unbypassed patients with associated CAD.

Patients with anterior septal defects benefited to a greater extent from bypassing associated CAD than did patients with posteriorly located septal defects (Fig 3). For example, after 5 years of follow-up 37% of patients who had unbypassed CAD and a posteriorly located VSD were alive, compared with 58% of patients who underwent bypass grafting and had a posteriorly located VSD. This is

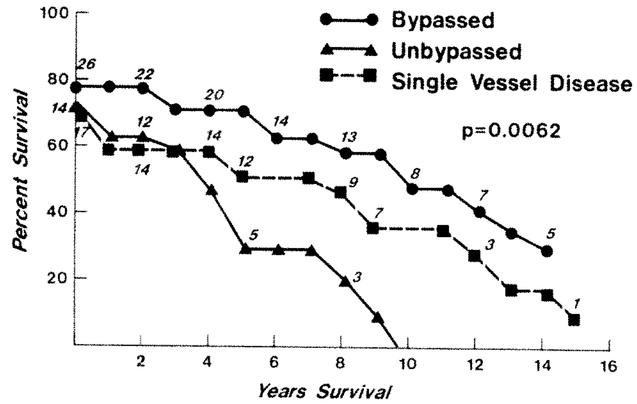


Fig 2. Long-term survival of bypassed patients (group 1), nonbypassed patients (group 2), and patients with single-vessel disease (group 3). Patient survivals between the three groups were different (p = 0.0062). There was no difference in survival at 10 and 15 years between the bypassed group and the group with single-vessel disease (p = 0.053). However, there was a significant difference between the bypassed and the unbypassed groups (p = 0.0015).

a difference of 21 percentage points or an improvement of 58% in survival. Whereas in patients with an anteriorly located VSD, only 16% of those with unbypassed CAD were alive after 5 years of follow-up, but after revascularization of all epicardial coronary disease, 92% were alive. This improved survival persisted after 10 and 15 years of follow-up for patients with a VSD in any location.

There was no significant difference in the number of patients with two- or three-vessel CAD undergoing CABG in the current era of coronary artery surgery (ie, since 1977, after the introduction of cardioplegia) compared with the group of patients not revascularized but with significant two- or three-vessel CAD ($p = 0.2$). Twelve patients (36.4%) with serious CAD underwent CABG before 1977 and 21 (63.6%) after. In the nonbypassed group with multivessel disease 10 patients (52.6%) underwent VSD repair before 1977 and 9 (47%) after. It is therefore unlikely that the bypassed patients benefited from being operated on later in our experience when our confidence with postinfarction septal defect repair was greater and when experience with coronary bypass operations, per se, was also greater. During the period of study, seven surgeons performed the operations. All had patients in groups 1, 2, and 3. There was no suggestion of bias toward bypassing or not bypassing associated CAD at the time of VSD repair.

The patients with bypassed CAD were similar in terms of preoperative age, sex, distribution of epicardial CAD, shunt ratio, and left and right heart filling pressures when compared with patients who had unbypassed CAD. Thus, the improved long-term survival of patients with bypassed CAD could not be explained by differences in the severity of CAD or known differences in the patient populations. It is unlikely that the two patients who underwent mitral valve replacement in group 2 adversely affected that group's overall long-term survival. One patient died after 12 months of a lymphoma and the other lived 44 months postoperatively before dying of a cerebral hemorrhage. Although 1 died early in the follow-up period, the other lived relatively long and acted to improve the group 2 overall survival.

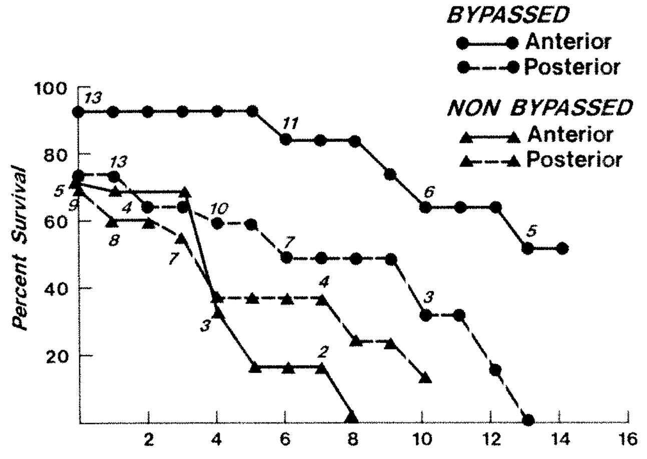


Fig 3. Long-term survival of bypassed (group 1) and nonbypassed patients (group 2) broken down by location of ventricular septal defect. Operative deaths are included in determinations.

Comment

Two- or three-vessel CAD occurred in 52 patients (69.3%) with VSD in our series. This is similar to the 61.2% incidence recently reported in several publications in which angiographic data were available (Table 5). Bypass grafts were placed in 33 of 52 of our patients (63.5%), a level that is also similar to the overall average rate of bypass grafting reported by other investigators (73.2%) [3–5, 11, 19–21]. The data presented in Table 5 were obtained from 8 of the most recently published articles that addressed the topic of postinfarction VSD and contained information relative to the incidence of angiography and bypass grafting of associated CAD.

Thus, CAD outside of the distribution of the infarct is commonly associated with postinfarction VSDs and represents a frequently encountered clinical problem in this group of patients. Previous authors have reported no differences in the *hospital mortality* of patients with or without CABG when undergoing VSD repair [3, 4, 11, 19–21]. These studies, however, have failed to separate out and compare patients with similar extent of CAD in the bypassed and unbypassed groups, and they therefore do not address the question of whether bypass grafting is truly beneficial based on a comparison of carefully matched cohorts. Furthermore, these studies did not look at the *long-term survival* of bypassed and unbypassed patients with similar degrees of CAD. Our relatively large group of patients with good long-term follow-up has allowed us to study these questions.

After separating out patients with single-vessel CAD, we were unable to demonstrate a difference in hospital survival between patients having bypass for two- and three-vessel disease and those not having bypass. Patients undergoing revascularization, however, demon-

Table 5. Incidence of CAD and Concomitant CABG in Recently Reported Series of Patients Undergoing Postinfarct Ventricular Septal Defect Repair

First Author	No. of Patients	Patients With 2- or 3-Vessel CAD	Patients Undergoing CABG	% of Candidates Actually Having CABG
Scanlon 1985 [4]	20	14 (70%)	11 (55%)	78%
Jones 1987 [3]	60	39 (65%)	14 (35.9%)	35.9%
Miyamoto 1983 [11]	8	6 (75%)	5 (67.5%)	83.3%
Von Segesser 1989 [19]	20	11 (55%)	10 (50%)	90.9%
Kennan 1983 [20]	34	N/A	13 (38.2%)	N/A
Weintraub 1983 [21]	12	10 (83.3%)	10 (83.3%)	100%
Skillington 1990 [5]	81	40 (49.4%)	32 (39.5%)	80%
Komeda 1990 [6]	31	22 (70.9%)	22 (70.9%)	100%
Total	266	142/232 (61.2%)	117/266 (43.9%)	104/142 (73.2%)

CABG = coronary artery bypass grafting; CAD = coronary artery disease.

strated significantly improved long-term survival when compared with patients who were unbypassed despite each group having a similar extent of CAD. Additionally, the lack of difference in long-term survival between unbypassed patients with single-vessel disease and those who were bypassed lends further support to the concept that revascularization may overcome the adverse effects of extensive CAD.

In patients with postinfarction ventricular septal rupture, CAD is etiologically related to the septal defect. Therefore, it is not surprising that survival is improved when the underlying problem is addressed. This recommendation is supported by previous reports of Czer and associates [22] and Chaffin and co-workers [23] in patients with ischemic mitral valve disease in whom mitral regurgitation was similarly caused by myocardial ischemia. Both groups documented an improved late survival in patients undergoing CABG when compared with patients not bypassed who had two- or three-vessel CAD. Moreover, Olearchyk and associates [24] have demonstrated an improved long-term survival in patients undergoing left ventricular aneurysmectomy when concomitant CABG was performed. Similarly, in our study, the addition of CABG improved late survival to the extent that survival was no different from that observed in patients with single-vessel CAD.

We have previously reported a generalized lack of collateral flow between the coronary arteries in patients suffering postinfarction VSD [25]. This observation might help to explain the benefit of complementary bypass grafting for patients undergoing VSD repair. The lack of collateral blood flow effectively separates regions of myocardium, and the additional blood provided by bypassing proximal stenoses may help to overcome the lack of collaterals. The poor long-term outcome of patients with unbypassed two- and three-vessel CAD supports a role for coronary arteriography in all patients being considered for VSD repair.

Patients with single-vessel CAD required fewer patches to repair the septum, indicating a smaller septal defect. Moreover, patients with single-vessel CAD suffered more anterior septal defects than the groups with more extensive coronary artery disease. This finding has been noted by others [5, 26]. Skillington and colleagues [5] proposed that because fewer patients with anterior myocardial infarction have two- or three-vessel disease than patients with posterior defects, only those patients with posterior septal defects should undergo coronary arteriography. Although we agree with Skillington and colleagues [5] and Smyllie and associates [26] that extensive CAD is less frequently associated with anteriorly located septal defects, we would disagree that this is a reason for selectively performing coronary angiography only on patients with posteriorly located defects. Both locations of septal defects benefited from bypass grafting. Furthermore, the patients with anterior defects benefited to a greater extent from bypass grafting than did the posterior defect group (see Fig 3). Therefore, all patients with postinfarction septal defects should undergo coronary artery angiography preoperatively.

We have seen an improvement in patient survival in more recent years, especially in the posterior septal defect group [2]. This is believed to be due to improved surgical techniques, earlier operation, and better perioperative management including improved myocardial protection. Even though it is not statistically significant, the apparent reason for the slightly higher hospital mortality in patients with single-vessel CAD compared with those who were bypassed may be explained by the fact that more patients with single-vessel disease were operated on earlier in our series (before 1975, $p = 0.055$). Others also have recently reported similar improved surgical results in these patients, which have been attributed to improved surgical and anesthetic methods [5].

We are unable exclude the possibility that the patients receiving CABG in addition to VSD repair were less ill in light of the fact that those patients had bypass grafting at the discretion of the attending surgeon. Careful analysis of our data does not suggest, however, significant demographic differences among the patient groups. Our data do suggest a survival advantage in patients with associated CAD who are bypassed in addition to having septal defect repair, thus supporting the use of coronary angiography preoperatively in all patients who have suffered postinfarction septal rupture.

Supported in part by a grant from Mr and Mrs Anthony A. Borgatti, Jr.

Our special thanks to Elizabeth Allred, MS, Statistician, Children's Hospital, Boston, Massachusetts, for her statistical help and to Stephanie Dailey for her secretarial help.

References

1. Oyamada A, Queen FB. Spontaneous rupture of the interventricular septum following acute myocardial infarction with some clinicopathological observation on survival in five cases. Presented at the first Pan-Pacific Pathological Congress, Tripler US Army Hospital, Honolulu, HI, Oct 12, 1961.
2. Daggett WM, Buckley MJ, Akins CW, et al. Improved results of surgical management of postinfarction ventricular septal rupture. Ann Surg 1982;196:269–77.
3. Jones MT, Schofield PM, Dark JF, et al. Surgical repair of acquired ventricular septal defect: determinants of early and late outcome. J Thorac Cardiovasc Surg 1987;93:680–6.
4. Scanlon PJ, Montoya A, Johnson SA, et al. Urgent surgery for ventricular septal rupture complicating acute myocardial infarction. Circulation 1985;72(Suppl 2):185–90.
5. Skillington PD, Davies RH, Luff AJ, et al. Surgical treatment for infarct-related ventricular septal defects: improved early results combined with analysis of late functional status. J Thorac Cardiovasc Surg 1990;99:798–808.
6. Komeda M, Fremes SE, David TE. Surgical repair of postinfarction ventricular septal defect. Circulation 1990;82(Suppl 4):243–7.
7. Gaudiani VA, Miller DC, Stinson EB, et al. Postinfarction ventricular septal defect: an argument for early operation. Surgery 1981;89:48–55.
8. Matsui K, Kay JH, Mendez M. Ventricular septal rupture secondary to myocardial infarction: clinical approach and surgical results. JAMA 1981;245:1537–9.
9. Kaplan MA, Harris CN, Kay JH, et al. Postinfarction ventricular septal rupture. Chest 1976;69:734.
10. Mattila J, Jarvinen A, Merikallio E, et al. Ischemic cardiac aneurysms and ventricular septal defects. Scand J Thorac Cardiovasc Surg 1980;14:257–62.
11. Miyamoto A, Lec M, Loess RM, et al. Post-myocardial infarction ventricular septal defect. J Thorac Cardiovasc Surg 1983;86:41–6.
12. Antman EM, Marsh JD, Green LH, Grossman W. Blood oxygen measurement in the assessment of intracardiac left to right shunts: a critical appraisal of methodology. Am J Cardiol 1980;46:265–70.
13. Heitmiller R, Jacobs ML, Daggett WM. Surgical management of postinfarction ventricular septal rupture. Ann Thorac Surg 1986;41:683–91.
14. Daggett WM. Surgical technique for early repair of posterior ventricular septal rupture. J Thorac Cardiovasc Surg 1984;84:306–12.
15. Daggett WM, Burwell LR, Lawson DW, et al. Resection of acute ventricular aneurysm and ruptured interventricular septum after myocardial infarction. N Engl J Med 1970;283:1507–8.
16. Duncan DB. *t*-Test and intervals for comparisons suggested by the data. Biometrics 1975;31:339–59.
17. Colton T. Statistics in medicine. Boston: Little, Brown, 1974.
18. Cox D, Oakes D. Analysis of survival data. London: Chapman and Hall, 1984.
19. Von Segesser LK, Siebenmann R, Schneider K, Jenni R, Gallino A, Turina M. Postinfarction ventricular septal defect—surgical strategies and results. Thorac Cardiovasc Surg 1989;37:72–5.
20. Keenan DJ, Monro JL, Ross JK, Manners JM, Conway N, Johnson AM. Acquired ventricular septal defect. J Thorac Cardiovasc Surg 1983;85:116–9.
21. Weintraub RM, Thurer RL, Wei J, et al. Repair of postinfarction ventricular septal defect in the elderly: early and long term results. J Thorac Cardiovasc Surg 1983;85:191–6.
22. Czer LS, Gray RJ, DeRobertis MA, et al. Mitral valve replacement: impact of coronary artery disease and determinants for prognosis of revascularization. Circulation 1984;70(Suppl 1):198–207.
23. Chaffin JS, Daggett WM. Mitral valve replacement: a nine-year follow-up of risks and survivals. Ann Thorac Surg 1979;27:312–9.
24. Olearchyk AS, Lemole GM, Spagna PM. Left ventricular aneurysm: ten years' experience in surgical treatment of 244 cases. Improved clinical status, hemodynamics, and long-term longevity. J Thorac Cardiovasc Surg 1984;88:544–53.
25. Miller SW, Dinsmore RE, Greene RE, Daggett WM. Coronary ventricular and pulmonary abnormalities associated with rupture of the ventricular septum complicating myocardial infarction. Am J Roentgenol 1978;131:571–7.
26. Smyllie J, Sutherland GR, Visser C, et al. Range of coronary artery lesions and the requirement for coronary angiography in post-infarct ventricular defects [Abstract]. Br Heart J 1989;61:114.

DISCUSSION

DR GREGORY LOUIS KAY (Los Angeles, CA): I thank The Society for the opportunity to open the discussion on this very important report and congratulate Dr Muehrcke on a very fine presentation. I would also like to thank Dr Daggett for forwarding to me a copy of the manuscript last week so that I could review it. At the outset, I would like to declare my colors. I must say I am among those Dr Muehrcke and associates referred to who do not believe angiography needs to be routinely performed preoperatively for patients with ruptured septum after infarction.

Fewer than 50% of patients with ruptured septum survive 1 week without operation. Ruptured septum is a surgical emergency. Acute renal failure and other signs of inadequate cardiac output are common. As Muehrcke and associates themselves point out, hospital survival for patients who undergo revascularization concomitant with ruptured septum repair is no better than for those who only have ruptured septum repair. We are all familiar with such patients who are destabilized by angiography. Patients with ruptured septum are marginally compensated, and angiography often results in further hemodynamic compromise. It is likely the sicker the patient, the more likely angiography will cause deterioration.

The question is one of hospital survival. Our report in 1981 showed a significant negative impact on survival for patients who underwent angiography before repair of ruptured septum. We still believe this is true.

Ejection fraction has been demonstrated to be an important determinant of long-term survivorship in these patients. A report by Jones from Manchester, England, in 1989 demonstrated that ejection fraction was the single most important determinant of long-term survivorship. In a cohort of 60 patients, all angiographically studied before repair of the ruptured septum, there was no long-term impact on survival with revascularization. Dr

Muehrcke, have you looked at your ejection fraction data, and what influence does ejection fraction have on your findings?

This study suggests a much better 5-year survival with concomitant revascularization, and indeed, 54% of late deaths in the nonrevascularized group were due to cardiac causes. It is not clear, however, what those cardiac causes were. Cardiac death in the study was defined either as recurrent rupture of the septum or residual septal defect, congestive heart failure, or myocardial infarction. Only infarction rate would be expected to be reduced with revascularization. It is also important to point out that of patients who were revascularized, about 44% also suffered late death due to cardiac causes. The question becomes: How many of these late deaths are actually controllable with concomitant revascularization?

Finally, 5 years is a long time. Even patients who have undergone straightforward revascularization are sometimes lost and are seen again only when they suffer recurrent infarction. Perhaps this problem is the same for patients who survive operation for ruptured septum. Our position is that all patients who survive operation for ruptured septum require catheterization between 3 and 6 months after operation. Don't these data really say that further close, long-term follow-up is needed to ensure good long-term survival?

DR MUEHRCKE: Thank you, Dr Kay. I will try and answer your questions, as I see them. We are familiar with the work out of Manchester looking at right ventricular ejection fraction as a predictor of long-term survival. We did not have those data available to us to look at and analyze. We think this is a very interesting topic and, perhaps, will look at this in the future; however, this does require biventricular angiography.

As far as long-term deaths, we did not see any ventricular ruptures in the late survival period. Most of the patch ruptures occurred early on, and the majority of patients who died late died of congestive heart failure or myocardial infarction. However, I hasten to add that the vast majority of patients who have survived this operation, and we have a woman who has survived now 24 years, are in New York Heart Association functional classification I or II; 80% or greater of the patients have very good results from this operation.

Just to give the audience a flavor of how frequently coronary angiography is performed and how frequently coronary artery bypass grafting is performed in patients currently, I would like to show a table (Table 5). This table demonstrates the eight most recent papers that have been written in the literature dealing with the topic of postmyocardial infarction ventricular septal defect rupture. I point out that the largest series is Skillington's series from Southampton. There were 101 patients in this series, 81 of whom underwent coronary artery angiography. As can be seen, 61% of patients in all the reports had two- or three-vessel coronary artery disease on angiography. Forty-three percent of the patients studied underwent coronary artery bypass grafting in addition to their ventricular septal defect repairs. Seventy-three percent of all patients with two- or three-vessel coronary artery disease actually underwent bypass grafting. Therefore, a substantial number of patients are currently undergoing coronary artery bypass grafting at the time of their septal defect repair. We are pleased to have demonstrated that these patients actually benefited from the added procedure.

DR ARMAND PIWNICA (Paris, France): I want to congratulate Dr Muehrcke for a very nice report, and I think it is proper to pay tribute to the Massachusetts General Hospital team for their contribution to the knowledge of this type of surgery. We published on the same subject in 1987 in *The Annals of Thoracic Surgery*. We reported our long-term results of emergency operation for postinfarction ventricular septal defect. The cases of 28 patients who survived emergency operation for postinfarction ventricular septal defect from 1970 to 1979 were reviewed. Only 1 patient had concomitant coronary artery bypass grafting, after only three coronary angiograms. Follow-up ranged from 7 to 16 years with an average of 10 years. There were four late deaths. Two were of cardiac origin: one was related to intractable congestive heart failure and one to malignant arrhythmia, and they occurred 1 and 6 years after operation, respectively. The other 2 patients died of noncardiac causes. Two patients required reoperation: 1 had a false aneurysm of the left ventricle that was resected 5 years after the initial operation. In the second patient unstable angina developed 10 years after closure of a ventricular septal defect and necessitated grafting of the left circumflex coronary artery. Both patients had an uneventful postoperative course.

Except for 1 patient who experienced an uncomplicated myocardial infarction 6 years after closure of the ventricular septal defect and the patient with unstable angina, the patients we followed up have remained up to now free from coronary events during follow-up. In fact, I do not know if there is a real discrepancy between our results and those of the Massachusetts General Hospital group because the site of the ventricular septal defect was anterior in 22 of our patients and inferior in 6 patients, with probably only one-vessel lesion for the patient with anterior ventricular septal defect.

I have been a little surprised by the time between diagnosis of a ventricular septal defect and time to operation. It is around 19 days for the three groups. Am I wrong or right?

DR MUEHRCKE: I believe that is correct.

DR PIWNICA: So when we operate on this type of patient we operate usually 48 hours after stabilizing the patient's condition with intraaortic balloon pumping, and if we get a nice stabilization we can perform coronary angiography. But our series of patients really consists of emergency patients operated on after 48 hours.

DR MUEHRCKE: Thank you for your comments. I would like to point out one very important point in the management of these patients, and that is that we do not wait on these people. We operate emergently. We believe that the long-term use of an intraaortic balloon pump to see if these patients' function improve is a failed therapy, and we operate as soon as possible. There are, as you can imagine, a group of patients who suffer postinfarction VSDs who have a small pulmonary to systemic blood flow ratio and who will be in fairly stable hemodynamic support and will not require emergency operation. But in general we operate as soon as we get these patients, and we are a referral center for these sorts of patients. We believe that the volume load is very hard for the heart to handle and in general we operate as soon as we can.

Risk Analysis of Operative Intervention for Failed Coronary Angioplasty

A. Michael Borkon, MD, Trent L. Failing, MD, Jeffrey M. Piehler, MD,
Duncan A. Killen, MD, Marcia L. Hoskins, BS, and William A. Reed, MD

Mid America Heart Institute, St. Luke's Hospital, Kansas City, Missouri

To assess the outcome of emergency coronary artery bypass grafting (CABG) after failed percutaneous transluminal coronary angioplasty (PTCA), 91 patients undergoing emergency CABG after failed PTCA over a 30-month period ending July 31, 1991, were studied. For reference, a cohort of patients (91) concurrently undergoing elective CABG equally matched for age, sex, number of grafts, ventricular function, and reoperative status was compared. Specific outcomes including death, hospital length of stay, use of blood products, and development of myocardial infarction were analyzed. More than half the patients undergoing emergency CABG for failed PTCA required three or more grafts. Operative mortality was 12.1% (11/99) for emergency CABG compared with 1% (1/91) for elective case-matched CABG patients (p = 0.007). Emergency CABG patients required frequent use of postoperative inotropes ($p = 0.02$) and intraaortic balloon counterpulsation ($p = 0.001$). Length of hospital stay ($p = 0.005$), administration of blood products ($p = 0.009$), postoperative myocardial infarction ($p = 0.0005$), and ventricular arrhythmias ($p = 0.0004$) were increased after emergency compared with elective CABG. The presence of multivessel disease or use of a reperfusion catheter had no influence on clinical outcome. Despite accumulated experience and improved operative management, patients requiring emergency CABG for failed PTCA remain at increased risk for postoperative complications and death.

(Ann Thorac Surg 1992;54:884–91)

The advent of percutaneous transluminal coronary artery angioplasty (PTCA) in 1977 dramatically changed the management of ischemic heart disease [1]. Although initially limited to single-vessel disease, it soon became a treatment option for patients with multivessel and even multilesion involvement. Subsequently, the clinical indications for PTCA have been extended to include patients with acute myocardial infarction, advanced age, poor left ventricular function, and prior coronary artery bypass grafting (CABG), and even patients not considered to be operative candidates [2]. Although early procedural success has been achieved in the majority of patients undergoing even "complex" PTCA, acute coronary artery occlusion has mandated emergency CABG in a small but persistent subset of patients. The present study was undertaken not only to contrast the results of truly emergency CABG for failed PTCA with an identically matched cohort of patients undergoing elective CABG, but also to determine specific preoperative clinical risk factors that might adversely influence postoperative outcome for emergency CABG after failed PTCA.

Material and Methods

Patient Population

From January 1, 1989, through July 31, 1991, 5,700 patients underwent PTCA at our institution. Of this number, 91 patients (1.6%) required emergency CABG within 24 hours of the PTCA procedure for signs and symptoms of unrelenting myocardial ischemia resulting from abrupt vessel occlusion, thrombosis, or coronary artery dissection (Table 1). Seventy-three (80%) patients went directly from the catheterization lab to the operating room. The remaining 18 patients had development of symptoms within 24 hours after PTCA necessitating emergency CABG. Electrocardiographic evidence of ischemia was usually present; however, routine 12-lead electrocardiograms were not always obtained in patients taken to operation directly from the catheterization laboratory. In these cases, clinical symptoms in conjunction with angiographic findings were enough to require emergency operative intervention.

Percutaneous transluminal coronary angioplasty was carried out as an emergency procedure in 33 patients (36%) as the initial acute intervention for myocardial infarction (MI). Thrombolytic agents were not used. The remaining 58 patients (64%) underwent PTCA as an elective procedure. Reoperative CABG was emergently carried out in 15 patients (16%).

After failed PTCA 28 patients (31%) had development of hypotension requiring inotropic drug support or intraaortic balloon counterpulsation (IABP). Emergency PTCA patients sustained hypotension more often than

---

Presented at the Thirty-eighth Annual Meeting of the Southern Thoracic Surgical Association, Orlando, FL, Nov 7–9, 1991.

Address reprint requests to Dr Borkon, Medical Plaza II, Suite 50, 4320 Wornall Rd, Kansas City, MO 64111.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Signs and Symptoms of PTCA Failure

Sign	No. of Patients (%)
Angina	47 (52)
Angina + hypotension	18 (20)
Angina + arrhythmia	16 (18)
Angina + hypotension + arrhythmia	7 (7)
Hypotension	2 (2)
Hypotension + arrhythmia	1 (1)
Total	91 (100)

PTCA = percutaneous transluminal coronary angioplasty.

those undergoing elective PTCA (15/33 [45%] versus 13/58 [22%]; $p = 0.04$) and required more frequent IABP (12/33 [36%] versus 9/58 [16%]; $p = 0.04$). Reperfusion catheters were placed in 30 patients (33%). Ventricular arrhythmias requiring intravenous lidocaine hydrochloride (Xylocaine; Astra Pharmaceutical, Westboro, MA), cardioversion, or cardiopulmonary resuscitation (CPR) occurred in 24 of 91 patients (26%). Eight patients required CPR on the way to the operating room, none of whom were undergoing reoperation.

Table 2 lists vessels compromised by PTCA. Myocardial ischemia resulted from occlusion of more than one vessel in 4 patients. In 6 patients, the left main coronary artery was inadvertently obstructed as a consequence of guidewire manipulation or retrograde dissection. Fifteen patients had undergone prior CABG. Emergency reoperation was carried out after failed PTCA of a diseased saphenous vein graft (6 patients) or native coronary artery (9 patients). These patients are listed in Table 2 according to native circulation compromised by PTCA.

Operative Technique

In the event that PTCA resulted in acute myocardial ischemia that could not be reversed by additional catheter intervention, the operating room was notified and an emergency surgical consultation obtained. To support a high-volume coronary angioplasty program, every attempt has been made to maintain an open operating room and available surgical personnel; however, the operating schedule occasionally mandated use of the next available operating room for these patients. In most cases, an attempt was made in the catheterization laboratory to establish some degree of vessel patency by placement of a guidewire or reperfusion catheter across the area of vessel compromise. Reperfusion catheters were placed in 30 (33%) of the patients with failed PTCA. The absolute duration of myocardial ischemia was frequently impossible to reliably quantitate due to multiple attempts to reestablish vessel patency in the catheterization laboratory, some of which were transiently successful.

Table 2. Vessel Compromised by Attempted PTCA

Vessel	No. of Patients (%)
Left anterior descending	44 (48)
Circumflex	18 (20)
Right coronary artery	19 (21)
Left anterior descending/circumflex	3 (3)
Left anterior descending/right coronary	1 (1)
Left main	6 (7)
Total	91 (100)

PTCA = percutaneous transluminal coronary angioplasty.

Inotropic drugs and IABP were employed when necessary to stabilize the patient's condition before transfer to the operating room. After induction of anesthesia, cardiopulmonary bypass was rapidly instituted and moderate systemic hypothermia (28° to 30°C) employed. Antegrade crystalloid or blood cardioplegia and, more recently, in selected cases, retrograde cardioplegia was administered after aortic cross-clamping to provide myocardial protection. Topical pericardial cooling was employed as an adjunctive measure. If more than one graft was necessary, the first graft carried out was usually to the compromised vessel, and additional cardioplegic solution was administered down the saphenous graft. With recent use of retrograde cardioplegia, supplemental cardioplegic delivery in this fashion was not performed. In all cases, complete revascularization was carried out. If stable hemodynamics were present and the electrocardiogram failed to reveal serious ischemic changes, the internal mammary artery was employed at the surgeon's discretion. In the setting of active ischemia or shock, no attempt was made to use conduits other than saphenous vein.

This group of patients undergoing emergency CABG was compared retrospectively with a cohort of 91 patients undergoing elective isolated CABG during the same period, equally matched for age, sex, ventricular function, number of grafts, and reoperative status. A perioperative MI was deemed to have occurred if diagnostic electrocardiographic findings (new Q wave or substantial reduction in R wave) were present in conjunction with total creatine kinase-MB (CK-MB) isoenzyme level of greater than or equal to 200 IU/L within 15 hours of CABG. Specific outcomes analyzed included death, length of hospital stay, use of blood products, and development of MI.

Statistical Analysis

Univariate comparisons between emergency CABG and elective CABG groups were carried out using Yates' corrected χ^2 analysis for discrete variables and two-tailed (pooled) unpaired Student's t test for continuous data (expressed as mean ± standard error of the mean). Continuous data were converted to dichotomous variables by selected cut-point determinations and retested by χ^2 analysis. All variables found to be of significance ($p < 0.05$) or marginal significance ($p < 0.1$) by univariate methods were then entered into a multivariate analysis. Stepwise multiple logistic regression analysis was performed to assess the independent contributions of multiple variables to development of specific outcomes. Statistical analysis was facilitated with the help of BMDP statistical software [3].

Table 3. Comparison of Preoperative Characteristics by Patient Group

Variable	Emergency CABG (n = 91)	Elective CABG (n = 91)	*p* Value
Age (y)	64 ± 1	63 ± 1	NS
Weight (kg)	81 ± 2	79 ± 2	NS
Ejection fraction	0.50 ± 0.01	0.49 ± 0.01	NS
Male	59 (65%)	59 (65%)	NS
Female	32 (35%)	32 (35%)	NS
Prior CABG	15 (17%)	15 (17%)	NS
Diabetes	19 (21%)	17 (19%)	NS
Prior MI	24 (26%)	40 (44%)	0.013
Prior PTCA	32 (35%)	25 (27%)	NS
Aortic cross-clamp (min)	44 ± 2	48 ± 2	NS
Bypass time (min)	76 ± 3	72 ± 3	NS
Number grafts (mean)	2.6 ± 0.1	2.8 ± 0.1	NS
LIMA/LAD (%)	22/70 (31%)	70/87 (81%)	0.0001
Postop inotropes	45 (50%)	29 (32%)	0.02
Postop IABP	29 (32%)	4 (4%)	0.0001
Postop VAD	2 (2%)	0 (0%)	NS

CABG = coronary artery bypass grafting; IABP = intraaortic balloon counterpulsation; LAD = left anterior descending; LIMA = left internal mammary artery; MI = myocardial infarction; NS = not significant; PTCA = percutaneous transluminal coronary angioplasty; VAD = ventricular assist device.

Results

Patient Characteristics

A comparison of selected preoperative and operative clinical variables is presented in Table 3. Except for an increased incidence of prior MI in patients undergoing elective CABG, both groups had comparable preoperative clinical characteristics. Fifteen patients in each group required reoperation. An identical average number of grafts was carried out for both cohorts. Forty-nine patients (54%) requiring emergency CABG for failed PTCA received at least three grafts. Single CABG was carried out in only 17 patients (19%). Similar durations of cardiopulmonary bypass and aortic cross-clamping were noted. Postoperative inotropic drugs or IABP or both were necessary in half of the patients undergoing emergency CABG. Seventeen of 33 patients (57%) undergoing CABG after failed emergency PTCA required postoperative IABP (12 preoperatively) compared with 12 of 58 patients (21%) after failed elective PTCA (9 preoperatively) ($p = 0.006$).

The left anterior descending coronary artery was grafted in 70 of 91 patients undergoing emergency CABG. An internal mammary artery was used in only 22 (31%) of these patients, compared with 70 of 87 (81%) in the elective CABG group who received a left anterior descending graft ($p = 0.0001$). Reperfusion catheters were in place in 23 patients who received left anterior descending grafts after failed PTCA. The internal mammary artery was used in 6 (26%) of these 23 patients. In the remaining 47 patients in the emergency CABG group requiring left anterior descending bypass who did not have a reperfusion catheter, 16 (34%) had internal mammary artery grafts carried out (p = not significant). Therefore, the presence of a reperfusion catheter alone was not influential in the decision to employ an internal mammary artery graft. Furthermore, use of a reperfusion catheter was not associated with an improvement in clinical outcome, mortality, or incidence of myocardial infarction. No differences could be found in any of the outcomes examined according to the location of the occluded coronary vessel. Furthermore, the extent of coronary artery disease and number of grafts were not significant determinants of morbidity or mortality.

Eighty percent of patients (73/91) undergoing emergency CABG were taken to the operating room directly from the catheterization laboratory. The remaining patients had development of unrelenting ischemia remote from the actual PTCA, but within 24 hours of the procedure. No significant difference in outcome was found between these two groups. Overall time from development of ischemia to arrival in the operating room had no bearing on the incidence of complications or death.

Reoperation was carried out in 15 patients (16%) undergoing emergency CABG. None of these patients required CPR after failed PTCA. There were four deaths in this group (27%). Inotropes were used in 10 patients (66%) and IABP was necessary in 8 (53%). In contrast, only 6 of 15 patients (40%) in the elective group undergoing reoperation required inotropes, and IABP was not necessary.

Mortality

Patients undergoing emergency CABG had a substantially greater risk of hospital death than elective CABG patients, 12.1% versus 1.1%, respectively ($p = 0.007$). One patient in each group could not be weaned from cardiopulmonary bypass and died intraoperatively. Deaths after emergency CABG for failed PTCA also included 4 due to low cardiac output, 5 due to multisystem organ failure and sepsis, and 1 due to mesenteric ischemia. In the emergency CABG group, all deaths occurred in patients who sustained considerable myocardial damage as manifest by postoperative electrocardiographic changes, elevated CK-MB isoenzyme levels, a need for postoperative circulatory support with inotropic agents or IABP, and a tendency for postoperative ventricular arrhythmias requiring treatment.

The risk of hospital mortality for patients undergoing emergency CABG was increased by weight less than 70 kg ($p = 0.04$), prior MI ($p = 0.009$), and need for preoperative inotropes ($p = 0.03$) or IABP ($p = 0.003$). Independent predictors of a fatal outcome determined by multivariate analysis were prior history of MI ($p = 0.003$) and preoperative IABP ($p = 0.002$).

Reoperative emergency CABG appeared to carry an increased hospital mortality (4/15; 27%) compared with nonreoperative patients (7/76; 10%), although not of significance by univariate analysis ($p = 0.14$). Likewise, operative risk seemed to be increased by preoperative CPR, but not significantly ($p = 0.08$). No difference was found in the number of grafts performed between survivors (2.7 ± 0.1) and nonsurvivors (2.8 ± 0.4). This

Table 4. Noncardiac Morbidity After Operation by Patient Group

Variable	Emergency CABG (n = 90)	Elective CABG (n = 90)	*p* Value
Renal failure	16 (18%)	4 (4%)	0.009
Respiratory failure	24 (27%)	1 (1%)	0.0001
Pneumonia	18 (20%)	2 (2%)	0.0004
Sepsis	8 (9%)	1 (1%)	0.04
Wound infection	10 (11%)	3 (3%)	NS
GI bleed	4 (4%)	0	NS
Stroke	7 (8%)	1 (1%)	NS
ICU stay (d)	6.2 ± 1.0	2.5 ± 0.2	0.0003
Total hospital stay (d)	15.9 ± 1.7	10.6 ± 0.5	0.005

GI = gastrointestinal; ICU = intensive care unit; NS = not significant.

observation was true whether the number of grafts was examined as a continuous or dichotomous variable.

Morbidity

Noncardiac causes of postoperative morbidity in operative survivors are listed in Table 4. Nearly all of these complications were much more common in patients undergoing emergency rather than elective CABG. In the emergency group, pneumonia or respiratory failure developed in a total of 26 patients (29%). Postoperative hospital length of stay was prolonged in patients undergoing emergency CABG ($p = 0.005$). By univariate analysis, preoperative hypotension ($p = 0.02$), inotropes ($p = 0.002$), IABP (0.004), female sex ($p = 0.014$), age greater than or equal to 65 years ($p = 0.03$), and left main involvement ($p = 0.05$) were associated with increased hospital stay. Multivariate analysis revealed preoperative shock ($p = 0.0001$), left main involvement ($p = 0.009$), and female sex ($p = 0.013$) to be independent factors increasing length of hospital stay in the emergency CABG group. Reoperation or number of grafts did not significantly influence the incidence of postoperative morbidity or length of stay.

Eight patients underwent CPR before emergency CABG with three postoperative deaths: two due to cardiac causes and one resulting from multiorgan failure. Neurologic complications were observed in 3 of 5 survivors. Hospital length of stay for survivors in this group ranged from 16 to 91 days (average, 40 days).

Blood Use

Despite the need for emergency operation and universal PTCA treatment with aspirin, dipyridamole (Persantine; Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT) and heparin, reexploration for bleeding was required in only 5 patients (6%) (Table 5). Thrombolytic agents were not administered to any patients undergoing emergency CABG. Although total chest tube drainage was similar between the elective and emergency CABG groups, blood use was increased in patients undergoing emergency CABG. Only 15% of these patients did not receive blood products compared with 33% of patients undergoing elective CABG ($p = 0.009$). Fresh frozen plasma and platelets were frequently used in the emergency CABG group.

Table 5. Blood Use by Patient Group

Variable	Emergency CABG	Elective CABG	*p* Value
Chest drainage (mL)	1,419 ± 131	1,274 ± 95	NS
Reoperation for bleeding	5 (6%)	4 (4%)	NS
Blood products	77 (85%)	61 (67%)	0.009
FFP/platelets	38 (42%)	19 (21%)	0.002
Blood (U)	6.1 ± 0.6	2.1 ± 0.2	0.0001

CABG = coronary artery bypass grafting; FFP = fresh frozen plasma; NS = not significant.

Univariate analysis determined that emergency CABG patients had an increased need for blood products if they were of age greater than or equal to 65 years ($p = 0.0006$), weight less than 70 kg ($p = 0.0001$), and female sex ($p = 0.007$). These variables, as well as the need for preoperative inotropic therapy ($p = 0.04$), were significant independent predictors of blood use.

Myocardial Infarction

The diagnosis of perioperative MI was made when electrocardiographic changes (new Q waves or R wave reduction) occurred in conjunction with an elevated CK-MB isoenzyme level (≥200 IU/L) (Table 6). Defined in this manner, an MI was determined to have occurred in 26 patients (29%) having emergency CABG, compared with 3 patients (3%) undergoing elective CABG ($p = 0.0005$). In the emergency CABG group, operation for failed emergency PTCA was an independent variable associated with an increased incidence of MI ($p = 0.0001$). Ventricular arrhythmias requiring treatment occurred in 25 patients (28%) undergoing emergency CABG, compared with only 6 elective CABG patients (7%) ($p = 0.0004$). The number of grafts performed and use of a reperfusion catheter or IABP had no impact on the incidence of MI.

Comment

Percutaneous transluminal coronary angioplasty has become a popular method of treatment for the management

Table 6. Postoperative Myocardial Infarction by Patient Group

Variable	Emergency CABG (n = 91)	Elective CABG (n = 91)	*p* Value
Total CK (IU/L)	2,159 ± 307	925 ± 62	0.0002
%CK-MB	9.4 ± 0.6	6.1 ± 0.4	0.0001
Total CK-MB (IU/L)	277 ± 93	62 ± 8	0.02
New Q/reduced R wave	46 (51%)	10 (12%)	0.01
Postoperative MI	26 (29%)	3 (3%)	0.0005
Ventricular arrhythmia	25 (28%)	6 (7%)	0.0004

CABG = coronary artery bypass grafting; CK = creatine kinase; MI = myocardial infarction.

of patients with ischemic heart disease. Because PTCA is promoted as a procedure of lesser morbidity and similar objective to CABG, most patients confronted with a treatment choice will opt for PTCA. This fact, coupled with technologic advances in the field of interventional cardiology, has helped to broaden both the acceptance of and indications for PTCA. Ryan and colleagues [4], in a task force report on PTCA, commented that "inherent to the strategy of coronary angioplasty is the price of failure." It is self-evident that, despite apparent improvements in technical success with PTCA, there will always be a group of patients who will require emergency CABG for ischemic complications of failed PTCA.

In the present series, only 1.6% of patients undergoing PTCA during the period of study required emergency CABG, a figure less than the 3.8% previously reported by our group in 1985 [5]. A similar reduction in the need for emergency CABG after failed PTCA was noted in a recent report of the National Heart, Lung and Blood Institute Registry of PTCA despite inclusion of high-risk patient subsets [6]. Presumably, operator experience and improved catheter techniques have helped to reduce but not eliminated the need for emergency operative intervention.

The present analysis, carried out over the past 2½ years, reflects a large practice of aggressive interventional cardiology. More than half of emergency CABG patients received at least three bypass grafts; only 19% had single-vessel involvement. The level of acuity and need for multiple grafts in this study contrasts with other reports [7–15].

Parsonnet and Greene and their colleagues have summarized previous reports of emergency CABG for failed PTCA [14, 15]. In a number of these studies, the definition of emergency CABG was quite broad, including true emergencies as well as urgent or same-day operations in stable patients [5, 8–11, 16]. All patients in the present study required true emergency operation for acute symptoms of myocardial ischemia ranging from unstable angina to MI despite maximal medical management. The majority of these patients were taken directly to the operating room from the catheterization laboratory, not infrequently in critical condition.

Previous studies in an attempt to contrast patients undergoing emergency CABG after failed PTCA with those undergoing elective CABG have used an assortment of control groups, often imprecisely matched or of a historical nature [5, 7–10, 12, 16–18]. To critically analyze clinical outcomes after emergency CABG, we included and compared a reference population of patients undergoing elective CABG closely matched for age, sex, extent of disease, ventricular function, and prior CABG undergoing CABG during the same period of study. Selection of cohort groups in this manner has previously been described [19].

Postoperative noncardiac morbidity in the present study was found to be increased after emergency CABG for failed PTCA. Multiorgan system failure including sepsis and renal and respiratory failure commonly led to increased lengths of hospital stay. As anticipated, these complications were frequently seen in the sickest patients with preoperative cardiogenic shock requiring inotropes or IABP. Although other investigators have described an increased frequency of postoperative complications in patients with multivessel disease [6, 7, 15], this finding could not be verified in the present study, presumably because of relatively few patients with single-vessel disease.

Operative mortality was also considerably higher for patients undergoing emergency CABG as compared with elective operation. This risk was found to be greatest among patients with failed PTCA who had experienced a previous MI or required preoperative IABP support due to cardiogenic shock [17]. Additional risk factors found by other investigators to be associated with increased mortality after emergency CABG include advanced age [6, 17], reduced ventricular function [6, 17], multivessel disease [6, 15], female sex [11], and prior CABG [6, 20]. Although not confirmed by the present study, a previous report from our institution did demonstrate that multivessel disease was associated with increased mortality but only by univariate analysis [5]. Again, the relatively small number of patients with single-vessel involvement in our study may not have permitted sufficient analysis of this variable.

Even though none of the patients in the present study received thrombolytics, the need for blood transfusions and administration of fresh frozen plasma and platelets was increased in patients undergoing emergency CABG [8, 10]. Presumably, antiplatelet agents and high doses of preoperative heparin led to increased intraoperative bleeding. Despite this finding, postoperative chest tube drainage and the incidence of reexploration for bleeding were not dissimilar for either the emergency or elective CABG group. As expected, patients found to be at increased risk for blood products administration were those who were in cardiogenic shock before operation or elderly women of low body weight.

The goal of emergency CABG after failed PTCA is to prevent or minimize myocardial injury. Unfortunately, divergent opinions exist regarding a uniform definition of perioperative MI. In a clinical pathologic study by Van Lente and colleagues [21], measurement of CK-MB isoenzymes at a level greater than 133 IU/L was 100% specific for myocardial damage observed at necropsy after unsuccessful CABG or valve operation. Experimental studies have demonstrated that reperfusion after temporary coronary vessel occlusion results in wash-out of CK-MB isoenzyme, which may exaggerate the measurement of CK-MB fraction [22]. In this study, infarction was determined to have occurred by the postoperative appearance of a new Q wave or substantial reduction in R wave in conjunction with a CK-MB isoenzyme fraction greater than 200 IU/L. Using this level of CK-MB, the number of patients in both groups who might be considered to have had a perioperative myocardial infarction may have been underestimated. However, as summarized recently by Greene and associates [15], the reported incidence of perioperative MI after emergency CABG for failed PTCA ranges from 18% to 51% with an average of 40%, consistent with our present observations.

A principal factor governing development of myocardial injury is the duration of ischemia before onset of reperfusion [23]. In the present study, the duration of ischemia could not be accurately determined as patients frequently underwent prolonged attempts to reopen occluded vessels, during which accurate assessment of ischemic time was not made. However, patients undergoing PTCA as emergency treatment of an acute MI who then required emergency CABG were found to be at increased risk for perioperative myocardial injury [10, 23]. These patients presumably incurred an additional ischemic time burden before undergoing ultimate revascularization. Several prior studies have found that multivessel coronary artery disease and multivessel PTCA were predictors of postoperative MI [7, 24]; however, our data did not confirm these observations. In the present study, preoperative ischemia or hemodynamic instability was not necessarily predictive of a postoperative MI, although this finding has been observed by others [12, 15, 17, 24].

The reperfusion or "bail-out" catheter has been proposed as a temporizing device to reduce or alleviate myocardial ischemia after failed PTCA [10, 25, 26]. Although we could not demonstrate a reduction in the incidence of MI, postoperative morbidity, mortality, or length of stay with use of this catheter, it was our observation that hemodynamic stabilization and temporary resolution of ischemia did occur on occasion, presumably due to the catheter's presence. Although this device alone did not result in increased use of the mammary artery, it may provide an increased opportunity for its use in selected patients [10, 25, 26].

Emergency reoperation in the setting of failed PTCA remains an operative challenge due to problems of urgent sternal reentry, difficulties achieving adequate myocardial protection, and potential for atheroemboli from diseased saphenous grafts. This group of patients tends to fare worse than the reoperative elective cohort in terms of postoperative requirement for inotropes and IABP, and in terms of subsequent postoperative complications [27]. Based on our prior experience, we do not take reoperative patients undergoing CPR to the operating room unless hemodynamic stability can be achieved [5]. The role of portable cardiopulmonary bypass remains uncertain in this setting [28].

Despite advanced age, reduced ventricular function, multivessel disease, reoperation, and even CPR, most patients in this study benefited from emergency operation after failed PTCA. However, the risk of postoperative complications, MI, and death for this group of patients remains substantial compared with that of patients undergoing elective CABG.

We gratefully acknowledge statistical advice from Lisa M. Soule, MA, and the secretarial support of Sharon Oliver.

References

1. Gruntzig A. Transluminal dilatation of coronary artery stenosis. Lancet 1978;1:263.
2. Holmes DR, Holubkov R, Vlietstra RE, et al. Comparison of complications during percutaneous transluminal coronary angioplasty from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung and Blood Institute percutaneous transluminal coronary angioplasty registry. J Am Coll Cardiol 1988;12:1149–55.
3. Dixon WJ, ed. BMDP Statistical Software Manual, Berkeley: University of California Press, 1990.
4. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). J Am Coll Cardiol 1988;12:529–45.
5. Killen DA, Hamaker WR, Reed WA. Coronary artery bypass following percutaneous transluminal coronary angioplasty. Ann Thorac Surg 1985;40:133–8.
6. Detre K, Holubkov R, Kelsey S, et al. Percutaneous transluminal coronary angioplasty in 1985–1986 and 1977–1981. The National Heart, Lung and Blood Institute Registry. N Engl J Med 1988;318:265–70.
7. Golding LAR, Loop FD, Hollman JL, et al. Early results of emergency surgery after coronary angioplasty. Circulation 1986;74(Suppl 3):26–9.
8. Brahos GJ, Baker NH, Ewy HG, et al. Aortocoronary bypass following unsuccessful PTCA: experience in 100 consecutive patients. Ann Thorac Surg 1985;40:7–10.
9. Connor AR, Vlietstra RE, Schaff HV, Ilstrup DM, Orszulak TA. Early and late results of coronary artery bypass after failed angioplasty. Actuarial analysis of late cardiac events and comparison with initially successful angioplasty. J Thorac Cardiovasc Surg 1988;96:191–7.
10. Pelletier LC, Pardini A, Renkin J, David PR, Hebert Y, Bourassa MG. Myocardial revascularization after failure of percutaneous transluminal coronary angioplasty. J Thorac Cardiovasc Surg 1985;90:265–71.
11. Cowley MJ, Dorros G, Kelsey SF, Van Raden M, Detre KM. Emergency coronary bypass surgery after coronary angioplasty: the National Heart, Lung and Blood Institute's percutaneous transluminal coronary angioplasty registry experience. Am J Cardiol 1984;53:22C–6C.
12. De Feyter PJ, van den Brand M, Jaarman GJ, van Domburg R, Serruys PW, Suryapranata H. Acute coronary artery occlusion during and after percutaneous transluminal coronary angioplasty. Frequency, prediction, clinical course, management and follow-up. Circulation 1991;83:927–36.
13. Stark KS, Satler LF, Krucoff MW, Rackley CE, Kent KM. Myocardial salvage after failed coronary angioplasty. J Am Coll Cardiol 1990;15:78–82.
14. Parsonnet V, Fisch D, Gielchinsky I, et al. Emergency operation after failed angioplasty. J Thorac Cardiovasc Surg 1988;96:198–203.
15. Greene MA, Gray LA, Slater AD, Ganzel BL, Mavroudis C. Emergency aortocoronary bypass after failed angioplasty. Ann Thorac Surg 1991;51:194–9.
16. Weintraub WS, Cohen CL, Curling PE, et al. Results of coronary surgery after failed elective coronary angioplasty in patients with prior coronary surgery. J Am Coll Cardiol 1990;16:1341–7.
17. Naunheim KS, Fiore AC, Fagan DC, et al. Emergency coronary artery bypass grafting for failed angioplasty: risk factors and outcome. Ann Thorac Surg 1989;47:816–23.
18. Ferguson TB, Muhlbaier LH, Salai DL, Wechsler AS. Coronary bypass grafting after failed elective and failed emergent percutaneous angioplasty. J Thorac Cardiovasc Surg 1988;95: 761–72.
19. Gardner TJ, Horneffer PJ, Manolio TA, et al. Stroke following

coronary artery bypass grafting: a ten-year study. Ann Thorac Surg 1985;40:574–81.
20. Edwards FH, Bellamy RF, Burge JR, et al. True emergency coronary artery bypass surgery. Ann Thorac Surg 1990;49:603–11.
21. Van Lente F, Martin A, Ratliff NB, Kazmierczak SC, Loop FD. The predictive value of serum enzymes for perioperative myocardial infarction after cardiac operations. An autopsy study. J Thorac Cardiovasc Surg 1989;98:704–10.
22. Jarmakani JM, Limbird L, Graham TC, Marks RA. Effect of reperfusion on myocardial infarct, and the accuracy of estimating infarct size from serum creatine phosphokinase in the dog. Cardiovasc Res 1976;10:245–53.
23. Phillips SJ, Zeff RH, Skinner JR, Toon RS, Grignon A, Kongtahworn C. Reperfusion protocol and results in 738 patients with evolving myocardial infarction. Ann Thorac Surg 1986;41:119–25.
24. Lazar HL, Haan CK. Determinants of myocardial infarction following emergency coronary artery bypass for failed percutaneous coronary angioplasty. Ann Thorac Surg 1987;44:646–50.
25. Kereiakes DJ, Abbottsmith CW, Callard GM, Flege JB. Emergent internal mammary artery grafting following failed percutaneous transluminal coronary angioplasty: use of transluminal catheter reperfusion. Am Heart J 1987;113:1018–20.
26. Sundram P, Harvey JR, Johnson RG, Schwartz MJ, Baim DS. Benefit of the perfusion catheter for emergency coronary artery grafting after failed percutaneous transluminal coronary angioplasty. Am J Cardiol 1989;63:282–5.
27. Lemmer JH, Ferguson DW, Rakel BA, Rossi NP. Clinical outcome of emergency repeat coronary artery bypass surgery. J Cardiovasc Surg 1990;31:492–7.
28. Kanter KR, Pennington DG, Vandormael M, et al. Emergency resuscitation with extracorporeal membrane oxygenation for failed angioplasty. J Am Coll Cardiol 1988;11:149A.

DISCUSSION

DR JAMES W. MACKENZIE (New Brunswick, NJ): I was particularly interested in the group that required cardiopulmonary resuscitation before going on bypass. Did you classify people in this category if they required only transient cardiopulmonary resuscitation, or indeed were these people who required cardiac massage until put on bypass? If it is the latter this is a very impressive salvage group.

DR ANDREW C. FIORE (St. Louis, MO): I rise to congratulate Dr Borkon and his associates from the Mid-America Heart Institute for their very poignant and timely analysis of patients requiring urgent revascularization after failed angioplasty, a problem that plagues all cardiac surgeons involved with the coronary bypass operation. Their results must be carefully appreciated, for they represent a well-established institution involved in the practice of aggressive interventional cardiology. Their overall operative mortality was 12%, and in patients requiring cardiopulmonary resuscitation or urgent reoperation after failed angioplasty, it rose to 40%. Their analysis demonstrates that the hemodynamic status of the patient at the time of operation is predictive of the clinical outcome.

I would like to discuss the experience at St. Louis University Hospital as of November 1991. We had approximately 200 patients having failed PTCA, which represents 4% of our angioplasty population. Our operative mortality was very similar to theirs, at about 10%.

The univariate analysis of risk factors that are predictors of operative mortality was similar to Dr Borkon's. Advanced age, more extensive coronary artery disease, left ventricular dysfunction, congestive heart failure, and hemodynamic instability were all predictors of operative mortality. The use of a perfusion catheter and the number of grafts performed at the time of urgent revascularization were not predictors of operative mortality. I have three questions for Dr Borkon.

Your policy states that emergency redo operation after failed angioplasty was not performed unless the patient could be successfully resuscitated. During your study interval how many patients in this category in fact could not be successfully resuscitated in the catheterization laboratory and presumably died? As a corollary, do you believe there may be a role for percutaneous extracorporeal support in the catheterization laboratory as a bridge to operation for patients in this emergency redo category? Now that you have analyzed your experience, can you offer us any practical guidelines for patients who are hemodynamically unstable and perhaps should not be taken from the catheterization laboratory to the operating room because of prohibitive mortality? Perhaps more importantly, what patients in your opinion should not receive surgical standby for PTCA in the first place?

Well-analyzed studies such as these are very timely in light of the recent state and federal scrutiny of the operative results for the coronary bypass operation.

DR RICHARD E. CLARK (Pittsburgh, PA): Dr Borkon, you are to be congratulated on analyzing your recent experience with excellent results. On the national scale there is a problem in defining groups of patients who have failed angioplasty. The first problem is that of the essentially dead patient in the catheterization laboratory and transfer of death from a medical unit to the operating room. Clearly, the surgeons take the brunt of the quality assurance problem. Therefore, we have been considering a category called resuscitation. How many of your patients were truly resuscitations?

My second question has to do with the definition of emergency. This has plagued us in the national database, because what is emergency to one group is not an emergency to another. We have defined this as requiring the first operating room available. How did you define the emergency patient in your analysis?

The last question concerns the patient who has had a prior cardiac operation who has a failed angioplasty. How were these handled in your series?

DR BORKON: Gentlemen, thank you for your kind comments. Let me address them in order.

Dr Mackenzie, we had 8 patients in this particular series who came to the operating room after having a period of cardiopulmonary resuscitation in the catheterization laboratory; of those 8 patients, 5 were undergoing cardiopulmonary resuscitation as they arrived in the operating room. None of those patients were reoperative cases. As a policy decision, because of our previous experience with the reoperative patient undergoing cardiopulmonary resuscitation, we have declined to take those individuals to the operating room unless their condition can be stabilized. Unfortunately, I do not know how many reoperative patients undergoing cardiopulmonary resuscitation were denied operation.

Dr Fiore, thank you for your comments. The St. Louis group is to be commended for their contribution in this area. Portable cardiopulmonary bypass system (CPS) has not been endorsed in our institution for several reasons. First, our cardiologists believe that they can manage most "complex" PTCAs without the need for CPS. Second, although we have discussed the merits in the setting of reoperation and the need for cardiopulmonary resuscitation, the logistics and the time involved setting up the CPS system are often greater than our ability to quickly get the patient down to the operating room. We maintain a floating, open operating room policy whereby in most cases we can rapidly transport these patients to the operating room and not have to wait for the next open operating room to become available. We do not provide surgical stand-by in the sense of preoperative consultations, even for critically ill patients.

Dr Clark, thank you for your comments. True emergencies were defined just as that: these were patients with acute myocardial ischemia, evolving myocardial infarction, or severe rest angina who were taken directly from the catheterization laboratory or in whom those symptoms developed within 24 hours after a PTCA and who were believed by their cardiologists and in consultation with surgical staff to be in impending danger of myocardial loss, and thus were dealt with expeditiously. Composition of the group requiring emergency CABG for failed angioplasty was two-thirds elective and one-third emergency PTCAs. Emergency PTCA was carried out for an evolving myocardial infarction and was the initial intervention. Only 7 of 33 of these patients undergoing emergency operation for failed emergency PTCA died.

Partial Median Sternotomy for Repair of Heart Defects: A Cosmetic Approach

William R. Wilson, Jr, MD, Michel N. Ilbawi, MD, Serafin Y. DeLeon, MD, William Piccione, Jr, MD, Kate Tubeszewski, RN, MSN, and Anthony F. Cutilletta, MD

The Heart Institute for Children, Oak Lawn, Illinois, and Rush Medical School, Chicago, Illinois

A modified median sternotomy incision that results in a cosmetically appealing scar is described. It includes the use of a low-lying short skin incision and partial transection of the sternum. The outcome in 182 infants and children indicates that this approach is safe, provides adequate exposure, and has excellent cosmetic results.

(Ann Thorac Surg 1992;54:892–3)

Median sternotomy is the preferred approach for cardiac procedures requiring cardiopulmonary bypass. It provides superior access for cannulation and exposure of intracardiac structures. A vertical incision beginning just below the suprasternal notch and extending to the xiphoid process is the typical skin incision used most commonly for median sternotomy. This incision leaves a long scar with poor cosmetic results. As increasing number of infants and children are undergoing repair of their heart lesions with very low operative mortality and morbidity, cosmetic outcome after cardiac operations in this age group has become increasingly important. Concern regarding postoperative scar appearance has stimulated the development and application of several alternatives to median sternotomy incision, none of which is without drawbacks.

We describe a new modification of the median sternotomy incision. It consists of a short low-lying midline incision and partial sternal transection. The technique provides adequate exposure for repair of intracardiac defects in infants and children with excellent cosmetic results.

Material and Methods

Population

From January 1986 to December 1990, 182 children between the ages of 2 days and 18 years have undergone total correction of a variety of intracardiac lesions using the technique described. Ventricular septal defects (70 patients, 38%) and atrial septal defects (54 patients, 30%) were the most common. A variety of other lesions were also approached through this incision: closure of atrial septal defect with relief of pulmonic stenosis, 12; aortic valvotomy, 18; closure of both atrial and ventricular septal defects, 16; relief of pulmonic stenosis, 7; and closure of ventricular septal defect with relief of pulmonic stenosis, 5.

Technique

A short midline incision centered over the lower one-third of the sternum is made (Fig 1). The subcutaneous tissue is dissected off the sternum from the level of the suprasternal notch superiorly to below the xiphoid inferiorly. The xiphoid process and linea alba are divided with cautery, and a curved scissors is used to develop a plane between

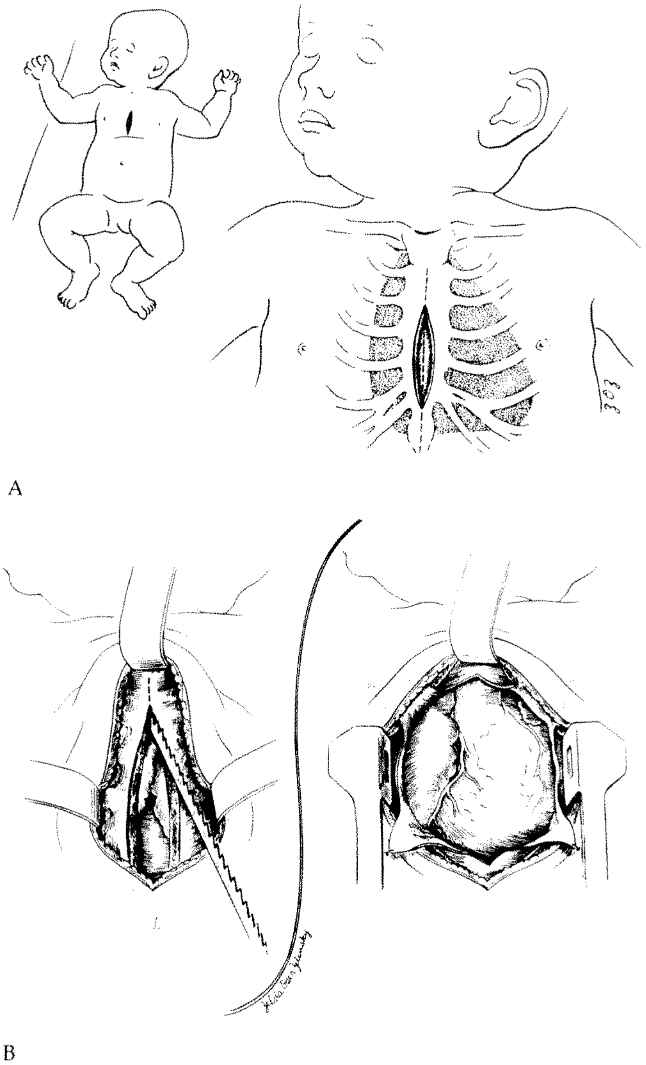


Fig 1. The typical incision is centered over the lower third of the sternum. Subcutaneous tissue is mobilized to the level of the manubrium, and the sternum is partially transected up to the sternomanubrial junction.

Accepted for publication Feb 28, 1992.

Address reprint requests to Dr Ilbawi, The Heart Institute for Children, Christ Hospital and Medical Center, 4440 W 95th St, Oak Lawn, IL 60453.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

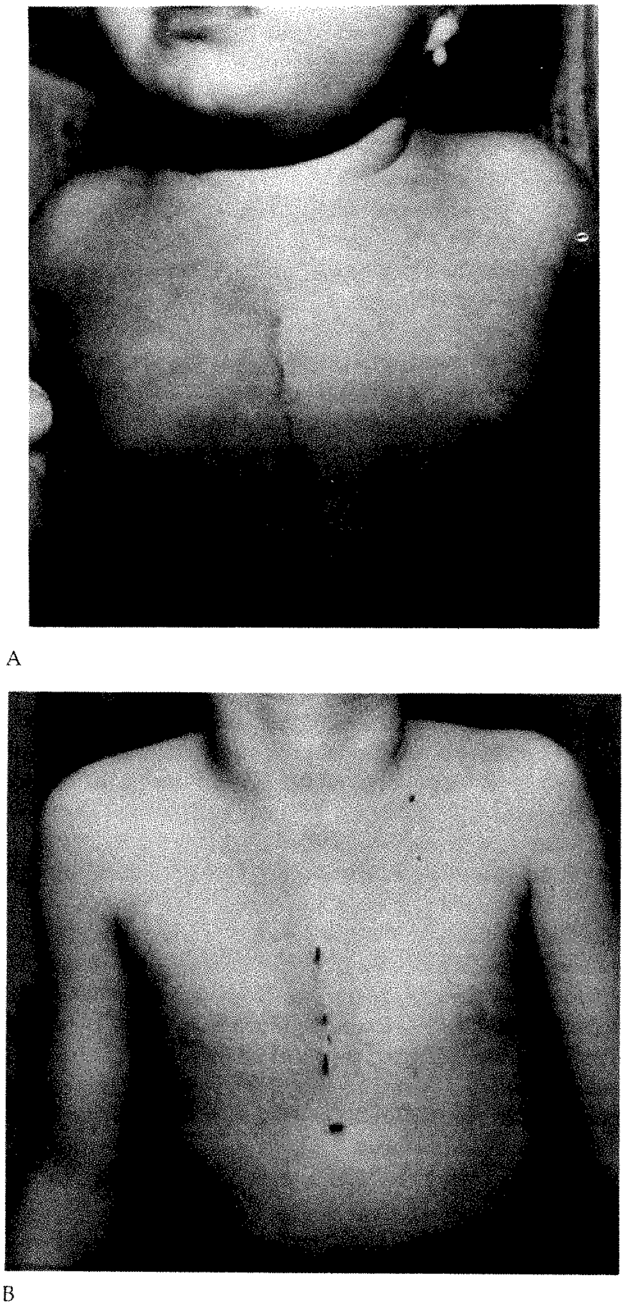


Fig 2. The length and location of the skin incision is shown in (A) a 6-week-old infant 2 months after an aortic valvotomy and (B) a 13-year-old girl 6 months after closure of an atrial septal defect.

the diaphragm and sternum. Straight heavy scissors in infants aged 1 month or younger, or a sternal saw in older children, is used to divide the lower two-thirds of the sternum from the xiphoid process up to, but not including the manubrium. A sternal retractor is placed and the sternum gradually opened. The thymus is mobilized and the pericardium incised. Pericardial traction sutures are applied in routine fashion with the sutures at the superior part tied to the subcutaneous tissue deeply underneath the mobilized skin (Fig 2). The aorta is mobilized to facilitate routine cannulation. The venous cannulas are inserted close to the cavoatrial junction. Caval exclusion is achieved by a 2-0 tie snugged around the vessels. The cut sternum is reapproximated in routine fashion after completion of the procedure.

Results

The length of the skin incision varied according to the size of the patient and the length of sternum (see Fig 1). Incisions ranged from 3.2 cm in neonates to 7.5 cm in older children. The length ratio of incision to total sternum varied between 0.32 and 0.47 (mean, 0.38 ± 0.2).

There was no hospital mortality. No patient had development of seromas, hematomas, sternal instability, or wound infection.

Comment

Several different approaches have been used to improve cosmetic results after cardiac operations. A bilateral horizontal submammary incision has frequently been used. However, this technique requires development of large subcutaneous flaps, which may predispose to impaired wound healing, hematomas, seromas, or maldevelopment and hypesthesia of breast tissue [1–3]. An inframammary incision with a right thoracotomy has also been used, particularly for repairing intracardiac lesions that require a right atrial approach. This approach has the disadvantages of increased pain associated with a thoracotomy, and a significant incidence of breast distortion due to scarring and fixation of the mobilized tissue.

The described technique with a short vertical skin incision and a partial sternotomy is a good alternative that can be performed easily in infants and young children with simple cardiac defects. Pliability of the skin and sternum in this age group allows such an approach without compromising surgical exposure. By retaining manubrial continuity, partial sternotomy aligns cut sternal edges accurately and provides immediate fixation of one-third of the sternum. Postoperatively, this decreases sternal instability and lessens sternal wound complications. The skin incision centered on the lower one-third of the sternum results in a small, well-hidden, cosmetically appealing scar, yet allows ample room to perform a variety of common intracardiac procedures. More complex operations requiring mobilization of the aortic arch, reconstruction of pulmonary arteries, or extensive exposure of intracardiac structures may necessitate a slightly larger skin incision and complete sternal transection.

References

1. Laks H, Hammond G. A cosmetically acceptable incision for the median sternotomy. J Thorac Cardiovasc Surg 1980;79:146–9.
2. De la Riviere AB, Brom GHM, Brom AG. Horizontal submammary skin incision for median sternotomy. Ann Thorac Surg 1981;32:101–4.
3. Bedard P, Keon WJ, Brais MP, Goldstein W. Submammary skin incision as a cosmetic approach to median sternotomy. Ann Thorac Surg 1986;41:339–41.

Surgical Considerations in Bypassing Coronary Arteries With 100% Proximal Occlusion

Thomas R. McLean, MD, Lars G. Svensson, MD, PhD, Bernardo Stein, MD,
Arthur C. Beall, Jr, MD, and John I. Thornby, PhD

The Cora and Webb Madding Department of Surgery and Department of Cardiology, Baylor College of Medicine, Houston, Texas

Objective data on the ability of cineangiography to predict the size of reconstituted totally occluded coronary arteries, as well as the clinical outcome of such revascularization, are sparse. Accordingly, we reviewed 200 consecutive cases of coronary revascularization to determine the answers to these questions. Group I patients (n = 57, with 86 totally occluded coronary arteries) had at least one coronary artery with a 100% proximal occlusion that reconstituted distally. Group II patients (n = 143, with 205 subtotally occluded coronary arteries) had 50% to 99% proximal stenosis of at least one coronary artery. Cineangiograms were blindly reviewed to measure the size of the coronary arteries, which were compared with the actual vessel size at operation. In group I, the totally occluded coronary arteries had a cineangiographic size of 1.9 ± 0.7 mm and an actual size of 1.6 ± 0.4 mm (p = 0.00004). In group II, the subtotally occluded coronary arteries had a cineangiographic size of 1.8 ± 0.4 mm compared with an actual size of 1.8 ± 0.3 mm (p = not significant). The site of bypass grafting was significantly smaller in group I (1.6 ± 0.4 mm versus 1.8 ± 0.3 mm; p = 0.00008). The two groups were similar with respect to preoperative and intraoperative parameters. Operative mortalities were similar (group I, 1.8%; group II, 3.5%; p = 0.68). Creatine kinase isoenzyme profiles and electrocardiographic changes were similar, except for a significant late rise of creatine kinase-MB in group I (56.1 ± 14.7 versus 30.7 ± 33.7 MIU/mL; $p < 0.001$). In conclusion, cineangiography significantly overestimates the size of totally occluded coronary arteries. The site of bypass in totally occluded coronary arteries is significantly smaller than in subtotally occluded arteries, and may result in an increased incidence of early graft closure, accounting for the late rise in creatine kinase-MB.

(Ann Thorac Surg 1992;54:894–7)

Frequently patients with coronary artery disease will be noted to have 100% proximal occlusion of one or more coronary arteries at the time of cardiac catheterization. When such an occluded vessel reconstitutes distally through collateral circulation, consideration is given to surgically bypassing this vessel.

The literature on the preoperative cineangiographic assessment of reconstituted coronary arteries is conflicting. Most investigators have found that the cineangiograms underestimate the actual size of reconstituted coronary arteries [1–4]. Pidgeon and colleagues [5], however, reported that the size of a reconstituted coronary artery at the time of the cineangiography accurately reflected the size of the vessel at the time of operation. Whether coronary arteriography accurately reflects the size of a reconstituted vessel is important because graft patency has been shown to be related to native vessel size [2, 3, 6, 7]. Accordingly, we have analyzed our most recent experience with patients undergoing coronary artery bypass to determine if coronary angiography accurately predicts the size of a reconstituted coronary vessel and to describe the clinical outcome of patients who have coronary artery bypass grafts to totally occluded vessels.

Material and Methods

The coronary cineangiograms of 200 consecutive patients undergoing coronary revascularization were reviewed in a blinded manner. Patients were divided into two groups depending on the extent of proximal coronary artery stenosis present. Group I (n = 57 patients) demonstrated at least one major coronary vessel that had a 100% proximal occlusion and that reconstituted distally through collateral circulation. Group II (n = 143 patients) consisted of patients who underwent coronary artery bypass for 50% to 99% proximal occlusion of at least one coronary artery. Patients undergoing a simultaneous valve procedure were excluded.

Cardiac catheterization was performed with an 8F Judkins catheter on a Phillips cardiac catheterization table. Multiple views of coronary vessels were obtained in the right anterior oblique and left anterior oblique projections. The site of bypass grafting was determined by diagrams of coronary anatomy made at the time of operation. The size of the coronary artery on the angiogram at the site where it was bypassed was measured by a blinded observer with a caliper. Magnification of the image was corrected for by the technique of Van Tassel and associates [8]. The calculated vessel size was compared with the vessel size determined at the time of operation. Actual coronary artery size was determined by the serial passage of coronary dilators into the vessel lumen. The largest dilator

---

Accepted for publication Feb 28, 1992.

Address reprint requests to Dr McLean, 6013 Leavenworth Rd, Kansas City, KS 66104.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Patient Profile

Variable	Group I (100% occlusion)	Group II (50% to 99% occlusion)
Sample Size		
Patients	57	143
Coronary arteries	86	205
Age (y)	59.3 ± 7.6	60.0 ± 8.3
Preoperative EF	0.50 ± 0.12	0.49 ± 0.12
Risk Factors (%)		
Diabetic	17.5	13.3
Hypertension	58.1	39.9
Smoking	66.4	54.5
Obesity	0.0	2.1
Family history	33.6	21.0
Hypercholesteremia	7.7	9.8
NYHA class (%)		
I	7.0	14.7
II	40.3	34.9
III	45.6	45.4
IV	7.1	5.0

EF = ejection fraction; NYHA = New York Heart Association.

Table 2. Characteristics of Operative Technique

Variable	Group I (100% occlusion)	Group II (50% to 99% occlusion)
No. of grafts per patient	2.8 ± 0.8	2.5 ± 0.8
No. of IMA grafts per patient	1.2 ± 0.7	1.1 ± 0.6
Cross-clamp time (min)	74.0 ± 23.7	63.9 ± 22.9
Pump time (min)	119.0 ± 35.7	107.4 ± 38.6

IMA = internal mammary artery.

that would comfortably enter the vessel lumen was considered the internal diameter.

Cardiac revascularization was performed in all patients at moderate systemic hypothermia with the heart arrested by cold antegrade crystalloid cardioplegia. Clinical parameters of preoperative risk factors and postoperative results were prospectively collected on all patients. Data are presented as the mean ± the standard deviation. Data were compared by Student's *t* tests and, where appropriate, by χ^2 analysis.

Results

Preoperative clinical parameters of cardiac risk were similarly distributed between the two groups (Table 1). All of our patients were male. The mean age of the two groups (group I, 59.3 ± 7.6 years; group II, 60.0 ± 8.3 years) as well as preoperative ejection fraction (group I, 0.50 ± 0.12; group II, 0.49 ± 0.12) were similar. The risk factors for coronary artery disease as well as New York Heart Association class were not significantly different between patients with total and subtotal occlusion.

The operative profiles of the two groups indicate that both groups were managed similarly (Table 2). In group I, the patients received 2.8 ± 0.8 grafts per patient and 1.2 ± 0.7 internal mammary arteries per patient. These figures are not significantly different from group II patients, who received 2.5 ± 0.8 grafts per patient and 1.1 ± 0.6 internal mammary arteries per patient. There was no significant difference in cross-clamp time (74.0 ± 23.7 minutes in group I versus 63.9 ± 22.9 minutes in group II) or in cardiopulmonary bypass time (119.0 ± 35.0 minutes in group I versus 107.4 ± 38.6 minutes in group II) between the two groups.

A total of 86 coronary arteries with complete proximal occlusion and distal reconstitution were present in the 57 patients in group I. Vessel size in these patients was compared with the vessel size obtained from another 205 bypassed vessels in group II patients that contained 50% to 99% (subtotal) proximal stenosis (Table 3). For vessels with 100% proximal occlusion the mean calculated reconstituted vessel size was 1.9 ± 0.7 mm compared with an actual size of 1.6 ± 0.4 mm ($p = 0.00004$). Thus, cinearteriography significantly overestimated totally occluded vessels by 0.3 ± 0.6 mm. The overestimate of size for the left anterior descending (0.2 ± 0.6 mm), marginal (0.4 ± 0.7 mm), and right (0.4 ± 0.5 mm) coronary arteries with 100% proximal occlusion was not significantly different. In patients with 50% to 99% proximal stenosis, cinearteriography predicted that the vessel size would be 1.8 ± 0.4 mm, whereas the actual vessel size was 1.8 ± 0.3 mm (p = not significant). Thus cinearteriography was inaccurate by only 0.0 ± 0.4 mm.

At the site of bypass grafting, the totally occluded vessels had an internal diameter that was significantly smaller than vessels with a subtotal occlusion (1.6 ± 0.4 mm versus 1.8 ± 0.5 mm; $p = 0.00008$). All but four vessels in group I were bypassed. In 2 of 4 patients, the reason the vessel was not bypassed was extensive calcification. In the remaining 2 patients, both calcification and small size (<1 mm) prevented bypass grafting.

The overall operative mortality in this series of 200 coronary revascularizations was 3%. Although the mortality rate in group II was twice that of group I, this difference was not significant (group I, 1.8%; group II, 3.5%; $p = 0.68$).

Postoperatively, the incidence of new Q waves was similar in both groups (group I, 5.2%; group II, 2.1%; p = not significant) (Table 4), as was the incidence of new right bundle-branch blocks (group I, 14%; group II, 10.5%; p = not significant). Elevation of total creatine kinase

Table 3. Vessel Comparison

Measurement	Group I (100% occlusion)	Group II (50% to 99% occlusion)
Calculated size (mm)[a]	1.9 ± 0.7	1.8 ± 0.4
Actual size (mm)	1.6 ± 0.4	1.8 ± 0.3[b]
Overestimated size (mm)	0.3 ± 0.6[c]	0.0 ± 0.4

[a] Based on measurements obtained by cineangiography. [b] $p = 0.00008$. [c] $p = 0.00004$.

Table 4. Myocardial Preservation

Variable	Group I (100% occlusion)	Group II (50% to 99% occlusion)
CK level (MIU/mL)		
Immediate total	962 ± 545	965 ± 735
Immediate MB	20.1 ± 13.6	31.3 ± 60.2
18-hour total	1,470 ± 1,321	1,407 ± 1,117
18-hour MB	56.1 ± 14.7	30.7 ± 33.7[a]
ECG		
New RBBB	14.0%	10.5%
New Q waves	5.2%	2.1%

CK = creatine kinase; ECG = electrocardiogram; RBBB = right bundle-branch block.

[a] $p < 0.001$.

enzyme level immediately upon arrival to the surgical intensive care unit was not significantly different between the two groups (group I, 962 ± 545 MIU/mL; group II, 965 ± 735 MIU/mL; p = not significant). The immediate postoperative absolute elevation in creatine kinase MB fraction was also similar (group I, 20.1 ± 13.6 MIU/mL; group II, 31.3 ± 60.2 MIU/mL; p = not significant). At 18 hours (late) postoperatively the total creatine kinase elevation remained similar between groups (group I, 1,470 ± 1,321 MIU/mL; group II, 1,407 ± 1,117 MIU/mL; p = not significant). There was a significantly greater rise in the late level of creatine kinase MB isoenzyme in group I compared with group II (56.1 ± 14.7 MIU/mL versus 30.7 ± 35.7 MIU/mL; $p = 0.001$). Moreover, within group I, this late elevation of creatine kinase MB isoenzyme was significantly increased from the initial postoperative value (20.1 ± 13.6 MIU/mL immediate postoperatively versus 56.1 ± 14.7 MIU/mL at 18 hours postoperatively; $p < 0.0001$).

Comment

Accurate interpretation of a cinearteriogram is important when planning a coronary artery bypass procedure, as early vessel patency is related to the size of the coronary vessel [2, 3, 6, 7]. It is widely believed among cardiac surgeons that the actual size of a distal coronary artery that has a 100% proximal occlusion is underestimated by cinearteriography. Van Tassel and associates [8] have suggested that the reason cinearteriography underestimated the actual size of the reconstituted vessel is that it represents a low pressure system.

Information on the accuracy of cinearteriography to assess the size of coronary arteries comes principally from two sources: (1) correlation of cinearteriogram with the findings at necropsy and (2) correlation of cinearteriographic studies before and after coronary artery bypass. McAlpin and others [9, 10] noted that the measured cinearteriographic size of normal coronary arteries was in close agreement with the size of coronary arteries obtained at postmortem examination. However, after reviewing 467 coronary arteries narrowed by more than 25%, Arnett and associates [11] concluded that the presence of diffuse coronary artery disease was the reason for the diminished coronary artery size found at the time of autopsy compared with the cineangiographic vessel size. A major limitation to these type of studies is that the cinearteriographic observations may have preceded the autopsy (or any subsequent cinearteriographic observations) by years.

Several studies involving cineangiography before and after coronary artery bypass have demonstrated that the reconstituted vessel lumen is underestimated by the preoperative cineangiography [1, 4, 6, 7]. Several problems exist with such a study design. First, only selected patients (generally those with symptoms) underwent arteriography postoperatively. Second, the studies were done at a variable time postoperatively. The variable time period allowed some bypassed vessels (under increased arterial pressure) to undergo progressive dilation.

After correlating the preoperative cinearteriogram with operative findings in 60 patients, Pidgeon and associates [5] concluded that the arteriographic image size was a good predictor of the coronary vessel size at the time of bypass. These investigators did not stratify their data by the degree of proximal stenosis. Moreover, Pidgeon and his co-investigators presented their data in terms of "angiographic predictive accuracy" and not in absolute size [5]. Our data in patients with subtotally occluded vessels confirmed their observation, as there was no significant difference between the cinearteriographic size and the coronary artery size found at the time of bypass when the vessel was only subtotally occluded proximally. However, our data indicate that cinearteriography significantly overestimates the actual vessel size when the vessel is completely occluded proximally. The absolute size of this overestimation (approximately 0.3 mm per vessel) may be small, but as seen in 2 of our patients, this overestimate may determine whether or not a vessel is bypassed.

In our practice the knowledge that cineangiography overestimates the size of reconstituted vessels has influenced us subtly. Reconstituted vessels are no longer assumed to be larger than their cineangiographic image.

It is not clear why cineangiography significantly overestimated the diameter of vessels with complete proximal occlusion. It may be that intraoperative spasm of totally occluded coronary arteries occurs to a greater extent than in subtotally occluded vessels. A more likely explanation is that incomplete visualization of the reconstituted vessel (due to low pressure or inadequate collateral flow) may not permit an accurate assessment of the vessel's caliber.

This study may be criticized because of the caliper method used to determine vessel size at angiography. However, the accuracy of caliper measurement is supported in the literature [12]. The major source of error is the fact that radiographic vessel images have edge gradients rather than a sharply demarcated edge [13]. Moreover, modern computerized techniques remain dependent on edge determination [14]. Despite this, the caliper technique remains operator-dependent as it relies on adjustment of magnification and assumes that the catheters are uniform in size [15]. Error may also have been introduced by comparing the quantitative caliper data with semiquantitative intraoperative measurements, under the assumption that operation itself did not alter vessel size. However, we believe that these potential errors in measurement would apply to both subtotally and totally occluded vessels. Further, these errors were minimized by the systematic methods used.

Quantitative angiographic methods were not used in this study. However, such state-of-the-art techniques are not available at every hospital. Clinically, we find that the caliper technique is readily available and practical.

Placement of a bypass graft to a reconstituted vessel results in regression of the collateral vessels that support the reconstituted portion of the coronary artery in the early postoperative period [16–19]. Despite this regression of collaterals, the literature on aortocoronary bypass to a reconstituted vessel indicates that such grafts have a reasonable patency. Nagaoka and associates [20] have published data that suggest that aortocoronary bypass grafts to completely occluded vessels have a patency superior to that found in similar bypass grafts to vessels with 50% to 99% occlusion. Rees [21] demonstrated in a study of 50 patients who underwent aortocoronary bypass that patency of vein grafts to completely occluded vessels was significantly better than that for vein grafts to vessels with subtotal occlusion. Our data indicate that totally occluded vessels are significantly smaller at the site of bypass grafting compared with subtotally occluded vessels. As graft patency has been demonstrated to be function of native vessel diameter, it would be expected that bypass grafts to totally occluded vessels would have a higher early closure rate [2, 3, 6, 7]. The late but significant rise in creatine kinase MB isoenzyme may in fact reflect a higher incidence of early graft closure in patients with totally occluded vessels. However, because of the format of this study (the lack of cineangiographic follow-up), whether there is an increased incidence of early graft closure in patients with smaller totally occluded vessels remains speculative.

In conclusion, we have observed that cineangiography significantly overestimates the size of a totally occluded coronary artery that reconstitutes distally. Moreover, the diameter of the coronary artery at the site of bypass grafting in totally occluded vessels is significantly smaller than the site chosen for bypass grafting in subtotally occluded vessels.

References

1. Cigarroa RG, Lange RA, Hollis LD. Quantitative assessment of coronary artery diameter before and after coronary artery bypass grafting. Am J Cardiol 1989;64:261–3.
2. Levin DC, Carlson RG, Baltaxe HA. Angiographic determination of operability in candidates for aorta coronary bypass. Am J Roentgenol 1972;116:66–73.
3. Rosch J, Dotter CT, Antonovic R, Bonchek L, Starr A. Angiographic appraisal of distal vessel suitability for aorta coronary bypass graft surgery. Circulation 1973;48:202–12.
4. Partridge JB, Brandt PW, Whitlock RM. The underfilled coronary artery: some pre and post operative observations on recipient arterial quality and left ventricular function after coronary artery surgery. Clin Radiol 1978;29:5–8.
5. Pidgeon J, Treasure T, Brooks J, Cattell M, Balcon R. Correlation of angiographic and surgical findings in distal coronary branches. Br Heart J 1984;51:125–9.
6. Walker JA, Frizdberg HD, Flemma RJ, Johnson WD. Determinants of angiographic pathway of aorta-coronary vein bypass grafts. Circulation 1972;45,46(Suppl 1, 2):86–90.
7. Morris GC Jr, Howell JF, Crawford ES, et al. Distal coronary bypass. Ann Surg 1970;172:652–60.
8. Van Tassel R, Moore R, Amplatz K. Determination of the true size of coronary artery in coronary arteriography. Am J Cardiol 1972;116:62–5.
9. McAlpin RN, Abasi AS, Grollman JH, Eber L. Human coronary artery size during life. Radiology 1973;108:567–76.
10. Baroldi G, Scomazzoni G. Coronary circulation in the normal and pathological heart. Wash Armed Forces Inst Pathol 1967;6:11.
11. Arnett EN, Isner JM, Redwood DR, et al. Coronary artery narrowing in coronary artery disease: comparison of cine angiographic and necropsy findings. Ann Intern Med 1979; 91:350–6.
12. Feldman RL, Peping CJ, Curry RC, Conti CR. Quantitative coronary arteriography using 105 mm photospot angiography and an optical magnifying device. Cathet Cardiovasc Diagn 1979;5:195–201.
13. Milne ENC, Friedman PJ. The role and performance of minute focal spots in roentgenology and special reference to magnification. Boca Raton, FL: CRC Publishing, 1971.
14. Herrold EM, Goldberg HL, Borer JS, Wong K, Moses JW. Relative insensitivity of densitometric stenosis measurement to lumen edge determination. J Am Coll Cardiol 1990;15: 1570–7.
15. Scoblionko DP, Brown G, Mitten S, et al. A new digital electronic digital caliper for the measurement of coronary arterial stenosis: comparison with visual estimates and computer-assisted measurements. Am J Cardiol 1984;53:689–93.
16. Watanabe N, Yonekura S, Williams AG Jr, Scheel KW, Downey HF. Regression and recovery of well-developed coronary collateral function in canine hearts after aorta-coronary bypass. J Thorac Cardiovasc Surg 1989;97:286–96.
17. Bourassa MG, Solignac A, Goulet C, Lesperance J. Regression and appearance of coronary collaterals in humans during life. Circulation 1974;50(Suppl 2):127–34.
18. McLaughlin PR, Berman ND, Morton BC. Saphenous vein bypass grafting: changes in native circulation and collaterals. Circulation 1975;52(Suppl 1):66–71.
19. Valle M, Wiljasalo M, Frock MH, Kochola O, Suoranta H, Tallroth K. Collateral circulation before and after coronary artery reconstruction. Ann Clin Res 1975;7:251–7.
20. Nagaoka H, Yano M, Tonouchi S, et al. The effects of aorto-coronary bypass grafting to totally occluded coronary arteries on left ventricular contractility. J Jpn Surg Soc 1985; 86:613–8.
21. Rees S. The watershed: a factor in coronary vein graft occlusion. Br Heart J 1976;38:197–200.

Role of Open Lung Biopsy in Diagnosing Pulmonary Complications of AIDS

Gregory D. Trachiotis, MD, Gordon H. Hafner, MD, William R. Hix, MD, and Benjamin L. Aaron, MD

Division of Cardiothoracic Surgery, George Washington University Medical Center, Washington, DC

Over a 4-year period, 25 patients with pulmonary complications of acquired immunodeficiency syndrome underwent open lung biopsy for diagnosis. Results of the biopsy led to a change in therapy in 15, and of this group, 8 patients improved clinically and were discharged. We believe that a select group of acquired immunodeficiency syndrome patients with pulmonary disease will benefit from open lung biopsy. Our indications for open lung biopsy are (1) a nondiagnostic bronchoscopy, (2) failed medical therapy after a diagnostic bronchoscopy, (3) failed empiric medical therapy after a nondiagnostic bronchoscopy or after a second nondiagnostic bronchoscopy, and (4) when any of the forementioned are accompanied with a worsening chest roentgenogram. Patients with acquired immunodeficiency syndrome who have a deteriorating respiratory status or require mechanical ventilation should not undergo open lung biopsy.

(*Ann Thorac Surg 1992;54:898–902*)

Approximately 50% of patients with the acquired immunodeficiency syndrome (AIDS) have development of pulmonary complications, with the majority due to *Pneumocystis carinii* pneumonia (PCP) [1–5]. Appropriate management of these patients is predicated on establishing the specific diagnosis of the pulmonary disease.

Since several studies have demonstrated that open lung biopsy (OLB) and bronchoscopy have nearly identical yields, particularly when the latter combines brushings, bronchoalveolar lavage, and transbronchial lung biopsy, there is considerable controversy over the role of OLB in these patients whose ultimate prognosis is fatal [3–8]. In patients with AIDS of longer than 1 year duration, the development of pulmonary disease results in 100% mortality. The median survival after an episode of PCP in patients with AIDS is 35 weeks; one-third of these episodes are fatal [3].

Surgeons are often called upon to perform OLB in patients with AIDS because bronchoscopy was not diagnostic or because there was no improvement, or even deterioration, despite accepted therapy for a pathogen diagnosed by bronchoscopy [3, 6, 9]. We herein report a review of our experience with patients with AIDS on a thoracic surgical service to determine if the morbidity, mortality, and clinical yield of OLB were justified by a change in management that favorably influenced the short-term outcome and survival. We will also comment on our current clinical and surgical approaches when considering an OLB in patients with AIDS.

Patients and Methods

Since 1983, there have been 553 admissions for 295 patients with AIDS to the George Washington University Hospital. Two hundred eighty-nine admissions were for pulmonary complications (53%). Of these, 25 patients were referred to the thoracic surgery service for biopsy. These patients were all male, with a mean age of 35 years. Nineteen were homosexual, 3 were bisexual, and 1 was both homosexual and an intravenous drug abuser. One patient claimed to be heterosexual with a female AIDS contact, and 1 denied all risk factors.

The admission diagnosis was PCP in 15 patients, Kaposi's sarcoma (KS) in 9, cytomegalovirus retinitis in 3, atypical *Mycobacterium* pneumonia in 1, cytomegalovirus esophagitis in 1, large cell lymphoma in 1, and *Cryptococcus* pneumonia in 1. Several patients had more than one diagnosis on admission. The average hospital stay was 22 days.

Biopsy techniques included OLB by limited thoracotomy in 17, OLB by thoracoscopy in 6, and mediastinoscopy in 1. One patient underwent thoracoscopy with conversion to thoracotomy after the initial technique was unsuccessful.

Indications for biopsy included nondiagnostic bronchoscopy with deteriorating pulmonary status in 15 and failure of medical therapy for a bronchoscopically established diagnosis in 7. Three patients who refused initial bronchoscopy underwent operation as their primary diagnostic procedure (2 OLB, 1 thoracoscopy). Twenty-two patients (88%) had at least one bronchoscopy before OLB.

Results

The pulmonary pathogens identified before and after OLB are listed in Table 1. The preoperative diagnosis was PCP

Accepted for publication March 2, 1992.

Address reprint requests to Dr Hix, Division of Cardiothoracic Surgery, George Washington University, 2150 Pennsylvania Ave, NW, Washington, DC 20037.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Pathogen or Disease Process Identified

Pathogen or Disease	Before OLB[a]	After OLB
PCP	7	11
KS	3	5
PCP + KS	1	. . .
MAI	. . .	1
NHL + KS	1	1
Lymphoma + CMV	. . .	1
Cryptococcus	. . .	1
No pathogen	15	4

[a] Diagnosis made principally by bronchoscopy, which may have been greater than one per patient.

CMV = cytomegalovirus; KS = Kaposi's sarcoma; MAI = *Mycobacterium avium-intracellulare*; NHL = non-Hodgkin's lymphoma; OLB = open lung biopsy; PCP = *Pneumocystis carinii* pneumonia.

in 7 patients, KS in 3, and lung abscess in 1. Fifteen patients had no specific preoperative diagnosis. The postoperative diagnosis was PCP in 11, KS in 5, and *Mycobacterium avium-intracellulare*, nonHodgkin's lymphoma plus KS, PCP plus KS, malignant lymphoma plus cytomegalovirus pneumonia, and *Cryptococcus* in 1 each. In 4 patients, no specific pathogen was found. The diagnostic yield for OLB was 21 of 25, or 84%.

The results of biopsy (Table 2) led to a change in therapy in 15 patients (60%). Of those with a therapy change, 8 (53%) improved clinically and were eventually discharged, 3 had no substantial change in their clinical status but were ultimately discharged, and 4 (26%) died. Of the 10 patients who had no change in their therapy after biopsy, 4 (40%) improved and were discharged, 1 was unchanged but eventually discharged, and 5 (50%) died. There was no statistical significance with regard to clinical improvement between those OLB patients who had a therapeutic change versus those who did not receive a change in therapy ($p = 0.547$ by Fischer exact test).

Complications occurred in 14 patients (56%). The most frequent complications were pneumothorax, persistent air leak, and difficulty with extubation. There were two deaths attributed to surgical care (8%). One of these involved a hypoglycemic complication of pentamidine therapy; the second was due to a tension pneumothorax after chest tube removal. Therefore, only 1 patient (4%) actually died due to a direct surgical procedure related to OLB. The seven other deaths were considered to be secondary to the progressive nature of the underlying disease. The total hospital mortality was 9 (36%).

Table 2. Outcome After Open Lung Biopsy

Variable	Therapy Change	No Therapy Change
No. of Patients (%)[a]	15 (60%)	10 (40%)
Clinical improvement and discharge	8 (32%)	4 (16%)
No clinical change and discharge	3	1
Total discharge per group	11/15 (73%)	5/10 (50%)
Mortality	4 (16%)	5 (20%)

[a] Percentages are based on a total of 25.

Comment

Open lung biopsy was first described in 1949 as a method for providing tissue for diagnosis of diffuse pulmonary infiltrates [10]. Long-term experience confirmed diagnostic yields of nearly 100%, operative mortality of less than 1%, and modest morbidity [11, 12]. Open lung biopsy was considered the diagnostic method of choice for diffuse pulmonary infiltrates of unknown etiology for a quarter century.

With the introduction of antineoplastic agents and immunosuppressive drugs for transplantation in the 1960s and 1970s, increasing numbers of patients underwent thoracotomy for diagnosis of opportunistic pulmonary infections. When fiberoptic bronchoscopy was introduced as a diagnostic technique in 1966, a controversy arose over whether this procedure or OLB was most appropriate for diagnosis of pulmonary infiltrates in immunocompromised patients. This debate continues in the present era of increasing numbers of AIDS patients with pulmonary complications.

Earlier proponents of OLB over fiberoptic bronchoscopy noted superior diagnostic yields, higher yield of treatable disease, and improved recovery, even in emergent situations [13–18]. In a prospective study in 1981, Burt and associates [14] concluded that OLB had significantly better diagnostic yield than aspiration needle, cutting needle, or transbronchial biopsy. Others, however, cautioned against excessive use of OLB [19, 20]. Although Rossieter and co-workers [21] reported a diagnostic accuracy of 97% with OLB, they noted that this resulted in change in therapy in less than half; moreover, the percentage of patients who improved was nearly the same regardless of whether a specific diagnosis was made. Hiatt and associates [22] also noted that OLB had only a modest impact on outcome, and McKenna and co-workers [7] concluded that although OLB seldom missed a specific, treatable cause, it only rarely produced a change in treatment that led to an improved clinical course.

At present, most authorities agree that the initial diagnostic approach in AIDS patients with pulmonary disease should be bronchoscopy. The refinement of bronchoscopic techniques, including the use of brushings, bronchoalveolar lavage, and transbronchial biopsy, has resulted in diagnostic yields in both retrospective and prospective studies that favorably compare with those of OLB, and with fewer complications [3, 5, 8, 23]. This is particularly true in the diagnosis of PCP. Open lung biopsy has been reserved for when bronchoscopy is not diagnostic or when the detected pathogen does not respond to appropriate therapy [5, 6, 24, 25].

A more important issue in the management of AIDS patients with pulmonary disease is not how the diagnosis should be made, but how much making a specific diagnosis benefits the patient. Robin and Burke [26] cited a series of retrospective studies on immunosuppressed patients in which survival was not improved after any form of lung biopsy. Pass and colleagues [25], in evaluating 23 OLBs in patients with AIDS, found that a therapeutic change was initiated in 67%. Outcome from these changes was not reported, however.

Our series of 25 patients with AIDS is one of the largest and most complete reports of OLB in this patient population. We found that despite most patients having had a prior bronchoscopy, 60% (15/25) had a therapeutic change after OLB. Of this group, 8 improved clinically and were discharged from the hospital. Thus, using the criteria of therapeutic change and subsequent clinical improvement, 8 of 25 patients (32%) did derive benefit from OLB. The overall mortality for patients undergoing OLB was 36%, but only 1 of 25 (4%) can be attributed to a direct surgical cause. Most deaths are due to the underlying disease process (7/25 patients), and thus a select group of patients with AIDS can tolerate OLB with an acceptable mortality and clinical outcome. Our series, like other similar ones, is limited by the number of patients to derive statistical significance, but this primarily reflects the limited number of patients with AIDS actually undergoing OLB. This limitation, however, does not undermine the important clinical concepts that can be valued from this study.

As in our group, a majority of patients with AIDS will succumb to their underlying disease process. Justice and associates [27] reported that about 40% of patients with AIDS die within 4 months, but about 25% can live more than 1 year. The prognosis is not necessarily based on the etiologic agent, but on how sick the patient has become. Therefore, for clinicians and surgeons, it becomes imperative to decide if short-term survival and quality of life can be improved with a more aggressive diagnostic approach. The issue then becomes which patients should receive an OLB.

During the past few years at the George Washington University Medical Center, there has been a trend toward a more aggressive nonsurgical diagnostic approach for AIDS patients with pulmonary complications. As clinicians and surgeons have gained experience in treating AIDS patients, some guidelines have been used in deciding on whom and when to perform surgical diagnostic procedures. These decisions are often formulated from input by medicine, oncology, radiology, pulmonary medicine, and surgical services.

A common approach at our institution for an AIDS patient with a pulmonary complication is to perform sputum analysis, chest roentgenography, and bronchoscopy. Almost all bronchoscopies are performed by our pulmonary medicine department. Bronchoalveolar lavage, brushings, and biopsy are common diagnostic techniques. In more than 97% of the cases, PCP can be diagnosed on bronchoalveolar lavage alone. The technique for bronchoalveolar lavage is fairly standard and consists of wedging the bronchoscope in the lobe of interest and instilling four 50-mL aliquots of normal saline solution with a subsequent one-third to one-half return. The effluent is sent for cytologic examination, in which routine staining techniques are employed. Specific stains for atypical bacteria, fungi, or viruses are left to the discretion of the medical team. Biopsy specimens are submitted for histologic examination and cultures as indicated. Improvement is based on symptomatic resolution, a clearing chest roentgenogram, and perhaps a repeat bronchoscopy to confirm adequate therapy.

In a number of patients, bronchoscopy may not yield a pathogen, yet a presenting abnormal chest roentgenogram usually warrants the initiation of empiric antimicrobial therapy. This scenario is exemplified in a small number of our patients (15/25) in whom even a repeat bronchoscopy failed to be diagnostic or yield a new pathogen. This does not reflect a failure in technique of bronchoscopy, but highlights a select group of patients whose infectious process becomes more elusive. Unfortunately, this is becoming a more common presentation, because many patients with the human immunodeficiency virus or AIDS are being placed on prophylactic antimicrobial therapy or are consequently being treated for one organism but may have other active pulmonary infectious processes. Frequently, our radiologists can give a differential diagnosis of a likely pathogen or disease process as their experience with AIDS patients has developed over the past decade. At times, a chest computed tomogram may be performed to evaluate the mediastinum, pleura, and lung parenchyma. If empiric therapy fails based on deteriorating clinical status and worsening radiologic survey, a repeat bronchoscopy will be attempted. Should the result again be nondiagnostic, the patient will then be referred for thoracic surgery consultation.

There is then another spectrum of patients whose clinical status deteriorates with or without a diagnosis, despite aggressive medical therapy or treatment of associative pulmonary complications, such as pneumothoraces or pleural effusions. Often these patients develop respiratory failure and may require mechanical ventilation. At this point, an intensive care unit admission may be warranted. Wachter and associates [28] have discussed some criteria used in deciding which patients should require intensive care unit care and its reliability to provide improved outcome. Our approach has been similar. We believe that when an AIDS patient's status deteriorates, issues regarding diagnostic procedures, predicted therapeutic outcome, prognosis and survival, and aggressive intensive care unit care, including mechanical ventilation, should be discussed with the patient. We believe this helps both patients and clinicians plan future treatment and evaluate its consequences.

The use of continuous positive airway pressure has averted intubation in a number of AIDS patients with hypoxia or respiratory failure. Our experience, like others [28, 29], has shown that AIDS patients with respiratory deterioration or mechanical ventilation have an overall mortality in the intensive care unit between 86% and 100%. Moreover, Peters and colleagues [29] reported a mortality of 91% for immunocompromised patients who required mechanical ventilation for pulmonary failure who underwent OLB for a diagnosis. It is clear that these types of patients should not undergo OLB. A final diagnosis in these patients may only be resolved at autopsy.

Thus, we believe there is a place for OLB in a select group of AIDS patients with pulmonary complications. Our criteria are as follows:

- Nondiagnostic bronchoscopy, with or without deteriorating clinical status
- Diagnostic bronchoscopy with failure to respond to medical therapy, with or without deteriorating clinical status
- Nondiagnostic bronchoscopy with empiric therapy based on radiologic survey with deteriorating clinical status
- Failure to yield a pathogen after repeat bronchoscopy or failure of radiologic improvement for any of the above
- Respiratory failure or mechanical ventilation are contraindications for open lung biopsy

At our institution, less than 5% of all admitted patients with AIDS and less than 10% of those with pulmonary complications will undergo OLB. Fiberoptic bronchoscopy with brushings, bronchoalveolar lavage, and transbronchial biopsy should be the initial diagnostic procedure. Routine chest roentgenogram and chest computed tomographic scan can provide additional diagnostic and therapeutic information. If this information is negative, then the patient will be evaluated by a thoracic surgeon for OLB. Most patients who undergo OLB will require a limited thoracotomy, but thoracoscopy can be less invasive and yield good diagnostic results (6/7 positive diagnosis in this series). Open lung biopsy is indicated when bronchoscopy is not diagnostic, when the patient's condition does not improve despite therapy for a pathogen diagnosed by bronchoscopy, when empiric therapy fails to improve a pulmonary process based on chest roentgenogram with a nondiagnostic bronchoscopy, and when a repeat bronchoscopy is nondiagnostic or fails to reveal a new pathogen. Although we believe the intensive care unit can provide short-term improvement in some AIDS patients with respiratory failure, we do not believe OLB can benefit these patients.

References

1. Gottlieb MS, Schroff R, Schanker HM, et al. *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a newly acquired cellular immunodeficiency. N Engl J Med 1981;305:1425–31.
2. Marchevsky A, Rosen MJ, Chrystal G, Kleinerman J. Pulmonary complications of the acquired immunodeficiency syndrome: a clinicopathologic study of 70 cases. Hum Pathol 1984;16:659–70.
3. Catterall JR, Potasman I, Remington JS. *Pneumocystis carinii* pneumonia in the patient with AIDS. Chest 1985;88:758–62.
4. Gottlieb MS. Pulmonary disease in the acquired immune deficiency syndrome. Chest 1984;86(Suppl):295–316
5. Hopewell PC, Luce JM. Pulmonary involvement in the acquired immunodeficiency syndrome. Chest 1985;87:104–12.
6. Murray JF, Felton CP, Garay SM, et al. Pulmonary complications of the acquired immunodeficiency syndrome: report of a National Heart, Lung, and Blood Institute workshop. N Engl J Med 1984;310:1682–8.
7. McKenna RJ, Campbell A, McMurtney MJ, Mountain CF. Diagnosis for interstitial lung disease in patients with acquired immunodeficiency syndrome (AIDS): a prospective comparison of bronchial washing, alveolar lavage, transbronchial lung biopsy, and open-lung biopsy. Ann Thorac Surg 1986;41:318–21.
8. Harman B, Koss M, Hul A, Baumann W, Athos L, Boyler T. *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome (AIDS): diagnosis with bronchial brushings, biopsy, and bronchoalveolar lavage. Chest 1985;87:603–7.
9. Fitzgerald W, Bevelaqua FA, Garay SM, Aranda CP. The role of open lung biopsy in patients with the acquired immunodeficiency syndrome. Chest 1987;91:659–61.
10. Klassen KP, Anlyan AJ, Curtis GM. Biopsy of diffuse pulmonary lesions. Arch Surg 1949;59:694–704.
11. Klassen KP, Andrews NC. Biopsy of diffuse pulmonary lesions: a seventeen-year experience. Ann Thorac Surg 1967;4:117–24.
12. Ray JF, Lawton BR, Myers WO, et al. Open pulmonary biopsy: nineteen-year experience with 416 consecutive operations. Chest 1976;69:43–7.
13. Greenman RL, Goodall PT, King D. Lung biopsy in immunocompromised hosts. Am J Med 1974;59:488–96.
14. Burt ME, Flye MW, Webber BL, Wesley RA. Prospective evaluation of aspiration needle, cutting needle, transbronchial, and open lung biopsy. Ann Thorac Surg 1981;32:146–53.
15. Leight GS, Michaelis LI. Open lung biopsy for the diagnosis of acute. diffuse pulmonary infiltrates in the immunosuppressed patient. Chest 1978;73:477–82.
16. Aaron BI, Bellinger SB, Shepard BM, Doohen DJ. Open lung biopsy: a strong stand. Chest 1971;59:18–22.
17. Nelems JM, Cooper JD, Henderson RD, Peng T, Phillips MJ. Emergency open lung biopsy. Ann Thorac Surg 1976;22:260–4.
18. Jaffe JP, Maki DG. Lung biopsy in immunocompromised patients: one institution's experience and an approach to management of pulmonary disease in the compromised host. Cancer 1981;48:1144–53.
19. Neff TA. Appropriate alternatives to open thoracotomy for diagnosis of pulmonary lesions. Ann Thorac Surg 1972;13:625–8.
20. Potter D, Pass HI, Brower S, et al. Prospective randomized study of open lung biopsy versus empirical antibiotic therapy for acute pneumonitis in nonneutropenic cancer patients. Ann Thorac Surg 1985;40:422–8.
21. Rossieter SJ, Miller DC, Chung AM, Carrington CB, Mark JBD. Open lung biopsy in the immunosuppressed patient: is it really beneficial? J Thorac Cardiovasc Surg 1979;77:338–45.
22. Hiatt JR, Gong H, Mulder DG, Ramming ITP. The value of open lung biopsy in the immunosuppressed patient. Surgery 1982;92:285–91.
23. Golden JA, Hollander H, Stulbarg MS, Gamsu G. Bronchoalveolar lavage as the exclusive diagnostic modality for *Pneumocystis carinii* pneumonia: a prospective study among patients with acquired immunodeficiency syndrome. Chest 1986;90:18–22.
24. McKenna RJ, Mountain CF, McMurtey MJ. Open lung biopsy in immunocompromised patients. Chest 1984;86:671–3.
25. Pass HI, Potter D, Shelhammer J, et al. Indications for and diagnostic efficacy of open-lung biopsy in the patient with acquired immunodeficiency syndrome (AIDS). Ann Thorac Surg 1986;41:307–12.
26. Robin ED, Burke CM. Lung biopsy in immunosuppressed patients. Chest 1986;89:276–8.
27. Justice AC, Feinstein AR, Wells CK. A new prognostic staging system for the acquired immunodeficiency syndrome. N Engl J Med 1989;320:1388–93.
28. Wachter RM, Luce JM, Lo B, Raffin TA. Life-sustaining treatment for patients with AIDS. Chest 1989;95:647–52.
29. Peters SG, Meadows JA, Gracey DR. Outcome of respiratory failure in hematologic malignancy. Chest 1989;94:99–102.

INVITED COMMENTARY

The increasing numbers of patients with AIDS in our population presents a burgeoning problem that taxes our clinical abilities to respond with cost-effective and appropriately timed therapeutic options. Pulmonary problems will develop in at least half of these patients in the course of their disease, confounded by the fact that 25% of these problems may be noninfectious in nature. Up to this point, a number of diagnostic tools have been employed, including bronchoscopy, sputum analysis, bronchoalveolar lavage, and transbronchial biopsy. Experience has also showed that the timing in the employment of diagnostic methods to institute specific therapy is very important in survival. Diagnostic measures including open lung biopsy and subsequent therapeutic interventions in patients with specific lung problems and ventilator-dependent respiratory failure do not affect survival. All reports so far have been retrospective in nature and always reveal a different mix of diagnostic measures and the timing of their use. Strategies are always evolving and are affected by considerations of cost-effectiveness, for both time and money, as well as the accuracy of diagnoses. Evaluations of diagnostic algorithms need to be done prospectively with our eye on outcome as the yardstick for comparison.

The noninvasive diagnostic methods have shown that they are as accurate as open lung biopsy with decreased morbidity and therefore should be employed before open lung biopsy. The clinical course of these patients dictates that these diagnostic methods be applied early because outcome is more related to the primary disease than to the pulmonary complications. Biopsy in a failing patient is of much less value if it indicates late institution of specific therapy.

This article reemphasizes the lessons that have been learned in the past and indicates that open lung biopsy is a way to provide a very specific diagnosis and can do so safely after other methods have failed. The fact that it is applied after all other methods have failed and in failing patients requires a dedicated and experienced surgical team to affect outcome favorably. It is probably the best method to diagnose Kaposi's sarcoma. The range of its applicability in hospitalized patients with AIDS at the present time is, as Trachiotis and associates indicate, 5% to 10%.

Nicholas P. Rossi, MD

Division of Cardiothoracic Surgery
The University of Iowa College of Medicine
Iowa City, IA 52242

Tetralogy of Fallot: Favorable Outcome of Nonneonatal Transatrial, Transpulmonary Repair

Tom R. Karl, MD, Shunji Sano, MD, PhD, Samphant Pornviliwan, MD,
and Roger B. B. Mee, FRACS

Royal Children's Hospital, Melbourne, Australia

This report describes our experience with 366 patients who had a transatrial, transpulmonary repair of tetralogy of Fallot between December 1980 and December 1991. Included in this group are patients with tetralogy of Fallot plus atrioventricular septal defect as well as patients displaying all degrees of aortic override (in the presence of subaortic ventricular septal defect and right ventricular outflow tract obstruction). Median age was 15.3 months and median weight, 12.3 kg. Of the 366 patients, 72% required a pericardial patch to reconstruct the main pulmonary artery or right ventricular outflow tract. Serious coronary anomalies were seen in 11 patients, without influencing surgical approach. There were two hospital deaths (0.5%; 70% confidence limits, 0.2% to 1.2%). Actuarial survival was 97.5% at 42 months (95% confidence limits, 95% to 99%) reflecting four late deaths over 1,129 patient-years of follow-up. Postoperative cardiac catheterization studies were performed in 61 patients at a mean follow-up interval of 23 months. Mean right ventricular/left ventricular systolic pressure ratio after repair was 0.46 (standard deviation, 0.28), and mean gradient across the right ventricular outflow tract was 15 mm Hg (standard deviation, 24 mm Hg). Actuarial freedom from reoperation for any reason has been 95% (95% confidence limits, 92% to 97%) at 5-year and 10-year follow-up. These early and medium-term results encourage us to continue with transatrial, transpulmonary repair of tetralogy of Fallot. We believe that this approach has an operative risk similar to or lower than transventricular repair, and that it will result in better preservation of right ventricular function in the long term.

(Ann Thorac Surg 1992;54:903–7)

Nearly 40 years have passed since Lillehei and associates' [1] first successful repair of tetralogy of Fallot (TOF) using cross-circulation. Since then, thousands of patients have undergone correction, and currently many pediatric cardiac centers are reporting excellent early results for repair of most TOF variants [2–6]. A major unresolved issue is the timing of operation relative to early and late survival, freedom from reoperation, and late functional status. Ideally, a repair should be designed and timed to offer low operative and late mortality, minimal attrition rate for children awaiting operation, preservation of anatomy and ventricular function, good early and late hemodynamic profile, and freedom from reoperation.

Hudspeth and associates [7] first reported the transatrial repair of TOF in 1963. Subsequently, it has been shown that TOF can be reliably repaired through a transatrial, transpulmonary approach [2, 5, 6, 8, 9]. Documentation of right ventricular (RV) dysfunction, pulmonary insufficiency, and ventricular arrhythmia after transventricular repair of TOF [2, 10–16] led us to adopt the transatrial, transpulmonary approach in 1980, and the results are reported herein.

Patients and Methods

In the interval spanning December 1980 to December 1991, 366 patients underwent transatrial, transpulmonary repair of TOF in our unit. Patients with pulmonary atresia and ventricular septal defect and patients with absent pulmonary valve syndrome were excluded from this series, as we consider them different from both an anatomic and physiologic point of view. Included were all TOF patients with pulmonary artery (PA) anomalies (hypoplasia, stenosis, discontinuity), atrioventricular septal defect, anomalous origin or course of a coronary artery, and all degrees of aortic override (double-outlet right ventricle with subaortic ventricular septal defect and right ventricular outflow tract obstruction [RVOTO]). Patients with double-outlet right ventricle and aortomitral discontinuity were excluded. Four patients operated on early in this period underwent a transventricular repair and are not included in this study. Since March 1981, all patients having operation for TOF in our unit were repaired using the transatrial, transpulmonary approach (n = 366).

The median age at the time of operation was 15.3 months. The age distribution is displayed graphically in Figure 1. Mean weight was 12.3 kg (standard deviation, 10 kg). Associated cardiac anomalies were present in 72 of 366 patients (20%):

Left superior vena cava	26
Persistent ductus	12
Secundum atrial septal defect	10

Accepted for publication March 2, 1992.

Dr Sano's current address is Okayama University Medical Center, Okayama, Japan.

Address reprint requests to Dr Karl, Victorian Paediatric Cardiac Surgical Unit, Royal Children's Hospital, Flemington Rd, Parkville, Victoria, Australia 3052.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

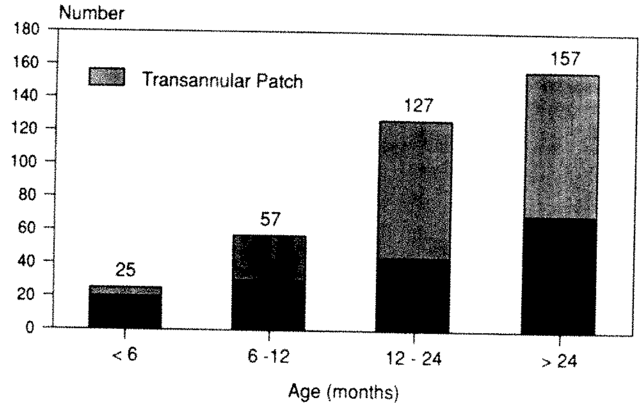


Fig 1. Age distribution of 366 patients undergoing transatrial, transpulmonary repair of tetralogy of Fallot. Transannular patch use is indicated for each age stratum.

Discontinuous left pulmonary artery	4
Interrupted inferior vena cava	3
Aortopulmonary window	1
Common atrium	1
Mitral stenosis/left ventricular hypoplasia	1
Straddling mitral valve	1
Partially anomalous pulmonary venous drainage	1
Totally anomalous pulmonary venous drainage	1
Complete atrioventricular septal defect	9
Anomalous coronary artery	11

One hundred thirty-five of 366 patients (37%) had undergone some form of previous palliation. Most of the palliative procedures (other than modified right Blalock-Taussig shunt) were performed in other units, the patients having been referred to us for intracardiac repair.

The operative technique was uniform throughout this 10-year period. Repairs were performed using hypothermic cardiopulmonary bypass with bicaval cannulation and cardioplegic arrest. Early in the series, circulatory arrest was used for parts of the repair in some patients. Systemic to PA shunts, if present, were divided after commencement of cardiopulmonary bypass. Working through the right atrium and tricuspid valve, we excised the parietal and septal extensions of the infundibular septum and carried dissection upward to the level of the pulmonary annulus. Other obstructing fibrous tissue and muscle bands were excised as well. Hegar dilators were passed through the tricuspid valve into the RV outflow tract to estimate its size. If the annular diameter at this point was less than the mean normal predicted by Rowlatt and colleagues [17] (as applied by Kirklin and associates [18]), then the main PA was incised. Valvotomy was performed through existing commissures whenever possible, and if necessary the incision was extended via the anterior commissure for 5 to 10 mm onto the RV free wall. The PA sizes were measured, and autologous pericardial patch enlargement was performed if required. Main PA and RV incisions were likewise repaired with a pericardial patch calculated to establish a diameter 2 to 3 mm larger than a normal main PA. Transannular patch use as a function of age at operation is displayed in Figure 1. Ventricular septal defects were closed transatrially, using interrupted pledgeted sutures and a Dacron patch. Other surgical procedures were performed as indicated for the coexisting cardiac defects. Significant coronary anomalies were encountered in 11 patients, including anomalous origin of the left anterior descending artery from the right coronary artery (n = 7), right coronary artery from left coronary artery (n = 3), and circumflex from right coronary artery (n = 1). The presence of the anomalous coronary artery did not influence the surgical approach. Six of these 11 patients required a transannular patch for relief of RVOTO.

Follow-up data were collected by ourselves or our referring cardiologists. Analysis of data was performed using Egret software (Statistics and Epidemiology Research Corp, Seattle, WA). Survival analysis employed the Kaplan-Meier technique, using 95% confidence limits (CL). Any patients lost to follow-up were censored from the analysis at the time of last follow-up. Proportion means are expressed with 70% CL with continuity correction for upper and lower limit.

Results

There were two hospital deaths, for an overall operative mortality of 0.5% (70% CL, 0.2% to 1%). The first occurred in a 15-month-old child with TOF plus anomalous origin of the left PA from the descending aorta, mitral stenosis, and small left ventricle. This child died of low cardiac output 24 hours after operation. The second occurred in a 4-month-old patient with TOF plus aortopulmonary window. He died suddenly of unknown causes the day after operation.

The 364 survivors have been followed up for a total of 1,129 patient-years (mean follow-up time, 37 months). Follow-up is complete for 92% of the patients. During this time there have been four late deaths documented. A 4-year-old patient with Down's syndrome and double-outlet right ventricle anatomy died of progressive pulmonary hypertension and pneumonia, probably on the basis of chronic upper airway obstruction. Postmortem examination showed grade 4 pulmonary vascular obstructive disease. A 6-month-old patient with Down's syndrome and complete atrioventricular septal defect plus TOF died suddenly at home 2 months postoperatively, 3 hours after administration of diphtheria/pertussis/tetanus vaccine. The third patient was a 21-month-old child with TOF plus bronchomalacia and spastic quadriparesis. He died 2 weeks after a reoperation for relief of left PA stenosis and pulmonary arteriopexy. His death is presumed to have been due to arrhythmia, and this was the only death after reoperation. The fourth patient was a 6-month-old baby who had been born prematurely and in whom bronchopulmonary dysplasia developed during a long period of ventilator dependence after birth. She had been on chronic oxygen therapy before and after TOF repair, which was done for relief of severe cyanotic spells. She died at home of respiratory failure related to infection, 6 months after repair.

The actuarial survival for all patients, including operative mortality, was 97.5% (95% CL, 95% to 99%) at 42 months with no deaths documented after that follow-up time (Fig 2). The great majority of survivors were in New York Heart Association class I at the time of most recent follow-up.

Postoperative cardiac catheterization studies have been performed in 61 patients at a mean interval of 23 months. This population is possibly skewed toward patients with suspected residual problems detected noninvasively, who were more likely to undergo catheter study earlier in the series. Systolic RV/left ventricular pressure ratio range was 0.17 to 1.2 (mean, 0.46; standard deviation, 0.28), with a systolic RV/PA pressure gradient of 0 to 90 mm Hg (mean, 15 mm Hg; standard deviation, 24 mm Hg). There was no difference in RV/left ventricular pressure ratio between patients with and without a transannular patch ($p > 0.05$). Although pulmonary insufficiency was detectable in a majority of patients, this was only rarely of important severity. Doppler echocardiographic studies were generally satisfactory in prediction of catheter findings, and are currently our main follow-up evaluation modality.

Reoperations have been required in 15 patients over this follow-up period. The indications for reoperation were as follows: ventricular septal defect, 3 patients; RVOTO, 6; PA branch stenosis, 2; ventricular septal defect and PA branch stenosis, 1; ventricular septal defect and RVOTO, 1; and RV outflow tract aneurysm, 2. Reoperations for residual RVOTO were performed through a ventriculotomy in 2 patients, but otherwise repeat transatrial approach was satisfactory. There was one reoperation-associated death, as mentioned in the discussion of late mortality. Actuarial freedom from reoperation for any reason was 95% (95% CL, 92% to 97%) at 5 years and 95% (95% CL, 87% to 98%) at 10 years (Fig 3).

Comment

The surgical risk for TOF repair is currently less than 5% in many centers [2, 5, 6]. Late results have also been good, with 20-year survivial often exceeding 90% [13, 19, 20]. These results have been marred, however, by a poor late hemodynamic status in some long-term survivors [2, 10, 11, 21–24]. Furthermore, sudden death from ventricular arrhythmia has been noted in 0.5% to 5% of patients within 10 years of operation [12–14]. Both late RV dilatation/dysfunction and an increased risk of ventricular ectopic activity are related, at least in part, to the presence of a large RV incision [2, 10, 11, 15, 19, 21–23]. In an attempt to minimize or avoid these problems, we adopted our current approach in 1980, encouraged by the results obtained in other units.

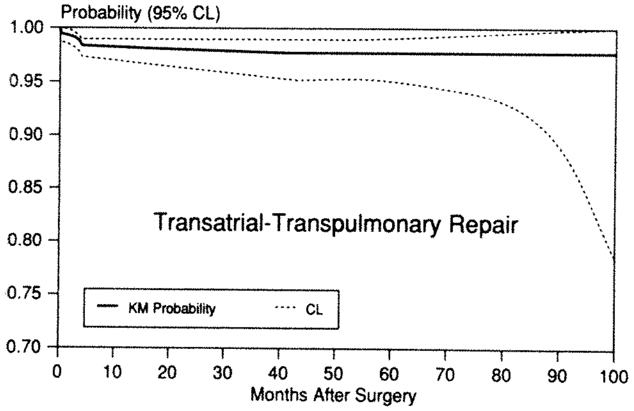


Fig 2. Kaplan-Meier (KM) actuarial survival for 366 patients undergoing transatrial, transpulmonary repair of tetralogy of Fallot. (CL = confidence limits.)

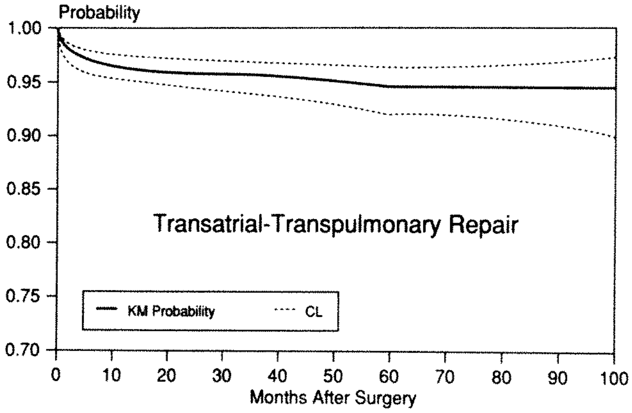


Fig 3. Kaplan-Meier (KM) actuarial freedom from reoperation for 364 hospital survivors of transatrial, transpulmonary repair of tetralogy of Fallot. (CL = confidence limits.)

Transatrial tetralogy repair differs from the classic approach in that the RV incision, if any, is just long enough to relieve the RVOTO. Ventriculotomy is therefore considerably shorter than would be required for ventricular septal defect closure, which can always be done transatrially in TOF. Kawashima and associates [2] have demonstrated that the transatrial, transpulmonary approach results in lower RV end-diastolic index and higher RV ejection fraction during isoproterenol infusion, as well as a lower ventricular arrhythmia incidence relative to the transventricular approach. Other studies have also suggested that arrhythmia problems could be decreased if the ventriculotomy were limited in size, although there are conflicting data on this point [15, 19, 24, 25]. Theoretically, with adequate relief of RVOTO, a competent or nearly competent pulmonary valve, and an intact right ventricle, patients without transannular patch (41% in our series) should have the maximum potential for good RV function. Even patients with a limited transannular patch should not develop severe pulmonary insufficiency, and in most cases we would predict a good probability of preserved RV function in the long term. As the transatrial, transpulmonary repair is suitable for all TOF variants (including cases with anomalous coronary arteries), we have used it exclusively since 1981.

A major question in the care of babies with TOF is when to operate. The detrimental effects of TOF (and cyanotic heart disease in general) on the myocardium, brain, lungs, and other organ systems are at least in part time-related [26–29]. Consequently, neonatal repair (for symptomatic and nonsymptomatic patients) has been advocated [30–32]. Success with neonatal repair of other lesions (for which delaying the operation is not an option) has provided some of the impetus [31]. In the long term, however, one must take into account attrition rate while awaiting operation, mortality after palliation, operative mortality, and late hemodynamic result. Although neonatal repair is attractive relative to the first two points, it remains to be seen whether the possibly higher operative mortality in this group will neutralize some of the (theoretical) benefits. Moreover, most neonatal repairs have been done using the transventricular approach, and therefore cannot solve the RV incision-related problems.

The transatrial, transpulmonary repair can be performed in any size child, but is technically more satisfactory in those weighing more than 6 to 8 kg. We have attempted to strike a balance between time-related complications of the disease and the likelihood of achieving a good technical repair without ventriculotomy. The mean age at operation has been lower in recent years, and our current practice is repair at around 10 to 15 months of age. Anatomically good candidates for transatrial, transpulmonary repair might have correction earlier if symptomatic. We also prefer to delay complete repair for patients with hypoplastic branch pulmonary arteries. Infants in this latter group have usually come forward for palliation before our usual elective correction age. The right modified Blalock-Taussig shunt remains our palliative procedure of choice for smaller or younger patients who are symptomatic but are not ideal candidates for transatrial, transpulmonary repair. These palliated children will also have complete repair at about 12 to 18 months of age.

Our nonneonatal one- or two-stage transatrial, transpulmonary repair has been satisfactory from the point of view of early and late mortality. Risk of palliation for TOF in our own unit (modified Blalock-Taussig shunt) currently approaches 0% (1 death in 10 years). The attrition rate of patients awaiting operation is difficult to know, as a substantial portion of our children are referred to us from other units (in and out of Australia) at the time of intracardiac repair. As the denominator in this group is unknown, the overall morbidity of waiting remains speculative. Certainly among patients followed up in our own cardiac unit from birth, the mortality is extremely low and mainly related to associated noncardiac problems. Although at this point it is impossible to prove statistically, our belief is that early and midterm resullts of our current program compare favorably with those of neonatal tetralogy repair in other units. As our follow-up is currently only approaching 10 years, we are unable to comment on the long-term outlook of transatrial repair relative to transventricular repair. We are aware that late hemodynamic deterioration (beyond 10 years' follow-up) that has been seen after transventricular repair is multifactorial and might occur with our approach as well.

As a final point, the transatrial, transpulmonary approach allows TOF repair in the presence of anomalous coronary arteries, which may be present in 2% to 9% of patients [33, 34]. Right ventricle to PA conduits were not required in any of our 11 patients, and the coronary arteries were preserved in all cases. Among these 11 patients, there have been no operative deaths and thus far only one reoperation for residual RVOTO.

In conclusion, we believe that this treatment program satisfies most of the criteria outlined in the introduction and will compare favorably with routine transventricular neonatal repair, in which a higher rate of RV dysfunction and late pulmonary insufficiency is projected, in addition to a (possibly) higher early mortality. We are aware that our follow-up time is limited and that the late hemodynamic deterioration based on other TOF-related factors may occur with our approach as well. Also, the overall mortality and morbidity for uncorrected patients in the first year of life remains somewhat speculative, although it has not been a major factor among patients followed up in our own unit. We, and many others, would therefore recommend nonneonatal transatrial, transpulmonary repair for children with TOF, as either a one-stage or, if necessary, a two-stage approach.

Some of the TOF operations in the earlier part of this series were performed by Mr William Brawn, currently Consultant Cardiac Surgeon in Birmingham, UK. Also, we acknowledge the role of our cardiologists, anesthetists, intensivists, nurses, and perfusionists in the management and care of these children.

References

1. Lillehei CW, Cohen M, Warden HE, et al. Direct vision intracardiac surgical correction of tetralogy of Fallot and pulmonary atresia defects. Report of first ten cases. Ann Surg 1955;142:418–45.
2. Kawashima Y, Kitamura S, Nakano S, Yagihara T. Corrective surgery for tetralogy of Fallot without or with minimal right ventriculotomy and with repair of the pulmonary valve. Circulation 1981;64(Suppl 2):147–53.
3. McGrath LB, Gonzalez-Lavin L. Tetralogy of Fallot repair with minimal or no ventriculotomy. J Cardiac Surg 1987;2: 27–47.
4. Pacifico AD, Sand ME, Bargeron LM, Calvin EC. Transatrial transpulmonary repair of tetralogy of Fallot. J Thorac Cardiovasc Surg 1987;93:919–24.
5. Dieth CA, Torres AR, Cazzaniga ME, Favaloro RG. Right atrial approach for surgical correction of tetralogy of Fallot. Ann Thorac Surg 1989;47:546–52.
6. Touati GD, Vouhé PR, Amodeo A, et al. Primary repair of tetralogy of Fallot in infancy. J Thorac Cardiovasc Surg 1990;99:396–403.
7. Hudspeth AS, Cordell AR, Johnston FR. Transatrial approach to total correction of tetralogy of Fallot. Circulation 1963;27:796–800.
8. Edmunds LH Jr, Saxena NG, Friedman S, Rashkind WJ, Dodd PF. Transatrial repair of tetralogy of Fallot. Surgery 1976;80:681–8.
9. Falkovskii GE, Ilin VN, Churkin VM, et al. Initial experience in the correction of the tetralogy of Fallot in infants using an approach through the right atrium and pulmonary artery. Grudn Serdechnososudistais Khir 1990;12:35–41.
10. Horowitz LN, Vetter VL, Harken AH, Josephson ME. Electrophysiologic characteristics of sustained ventricular tachycardia occurring after repair of tetralogy of Fallot. Am J Cardiol 1980;46:446–52.
11. Harkin AH, Horowitz LN, Josephson ME. Surgical correction of recurrent sustained ventricular tachycardia following complete repair of tetralogy of Fallot. J Thorac Cardiovasc Surg 1980;80:779–81.

12. Foster V, McGoon DC, Kennedy MA, et al. Long term evaluation (12–22 years) of open heart surgery for tetralogy of Fallot. Am J Cardiol 1980;46:625–82.
13. Katz NM, Blackstone EH, Kirklin JW, et al. Late survival and symptoms after repair of tetralogy of Fallot. Circulation 1982;65:403–10.
14. Rosing DR, Borer JS, Kent KM, et al. Long term hemodynamic and electrocardiographic assessment following operative repair repair of tetralogy of Fallot. Circulation 1978;58:(Suppl 1):209–17.
15. Basagoitia AM, Iturralde P, Galvan O, et al. Disorders of the rhythm and conduction in patients operated on for a total correction of tetralogy of Fallot. Arch Inst Cardiol Mex 1991;61:27–32.
16. Zimmermann M, Friedli B, Adamec R, Oberhansli I. Ventricular late potentials and induced ventricular tachycardia after surgical repair of tetralogy of Fallot. Am J Cardiol 1991;67:873–8.
17. Rowlatt JF, Rimoldi HJA, Lev M. The quantitative anatomy of the normal child's heart. Pediatr Clin North Am 1963;10:499.
18. Kirklin JW, Barratt-Boyes BG. Ventricular septal defect and pulmonary stenosis or atresia. In: Kirklin JW, Barratt-Boyes BG. Cardiac surgery. New York: Wiley, 1986:701–99.
19. Kawashima Y, Kobayashi J, Matsuda A. Long term evaluation after correction of tetralogy of Fallot. Kyobu Geka 1990;43:660–5.
20. Miyamura H, Eguchi S. Long term follow-up (20–25 years) of tetralogy of Fallot after correction. Kyobu Geka 1990;43:640–4.
21. Korns ME, Schwarz CJ, Lillehei CW, Edwards JE. Sequelae and complications of ventriculotomy. A pathologic study. Circulation 1969;39(Suppl 3):124–7.
22. March HW, Ross JK, Weirich WL, Gerbode F. The influence of the ventriculotomy site on the contraction and function of the right ventricle. Circulation 1961;24:572–7.
23. Stirling GR, Stanley PH, Lillehei CW. The effects of cardiac bypass and ventriculotomy upon right ventricular function. Surg Forum 1957;8:433–8.
24. Kato H, Nakano S, Matsuda H, et al. The influence of pulmonary regurgitation on left ventricular function after repair of tetralogy of Fallot. Nippon Kyobu Geka Gakkai Zasshi 1990;38:2257–63.
25. Abe T, Komatsu S. Long term followup studies in 211 patients with tetralogy of Fallot after corrective surgery over ten years. Kyobu Geka 1990;43:598–604.
26. Yamaki S. Pulmonary vascular disease in shunted and non-shunted patients with tetralogy of Fallot. Tohoku J Exp Med 1990;162:109–19.
27. Hausdorf G, Hinrichs C, Nienaber CA, Keck EW. Left ventricular contractile state after surgical correction of tetralogy of Fallot: risk factors for late left ventricular dysfunction. Pediatr Cardiol 1990;11:61–8.
28. Chandar JS, Wolff GS, Garson A Jr, et al. Ventricular arrhythmias in postoperative tetralogy of Fallot. Am J Cardiol 1990;65:55–61.
29. Li RK, Mickle DA, Weisel RD, et al. Effect of oxygen tension on the antioxidant enzyme activities of tetralogy of Fallot ventricular myocytes. J Mol Cell Cardiol 1989;21:567–75.
30. Guirgis NH, Losay J, Serraf A, et al. Complete repair of tetralogy of Fallot in infants under the age of six months. Arch Mal Coeur 1991;84:679–83.
31. Di Donato RM, Jonas RA, Lang P, et al. Neonatal repair of tetralogy of Fallot with and without pulmonary atresia. J Thorac Cardiovasc Surg 1991;101:126–37.
32. Gay F, Guarnera S, Tamisier D, et al. Results of the surgical treatment of tetralogy of Fallot before six months of age. A consecutive series of 62 cases with 49 complete repairs. Arch Mal Coeur 1990;83:511–6.
33. Fellows ICE, Freed MD, Keane JF, Van Praagh R, Bernhard WF, Castaneda AL. Results of routine preoperative coronary angiography in tetralogy of Fallot. Circulation 1975;51:561–6.
34. Hurvitz RA, Smith W, King H, Girod DA, Caldwell RL. Tetralogy of Fallot with abnormal coronary artery. J Thorac Cardiovasc Surg 1980;8:129–34.

Benefits of Combined Balloon Pumping and Percutaneous Cardiopulmonary Bypass

Steven J. Phillips, MD, Robert H. Zeff, MD, Chamnahn Kongtahworn, MD,
André Grignon, MD, Lawrence Barker, RN, L. A. Iannone, MD,
Mark Tannenbaum, MD, Margaret H. Verhey, MD, William J. Wickemeyer, MD,
Magdi G. Ghali, MD, and David F. Gordon, MD

Cardiovascular Medicine and Surgery Department, Mercy Hospital Medical Center, Des Moines, Iowa

Sixteen patients (2 women, 14 men) aged 29 to 72 years with continued cardiogenic shock during intraaortic balloon pumping (IABP) had additional treatment with percutaneous cardiopulmonary bypass (PBY). Cause of cardiogenic shock was myocardial infarction in 7 (3 survived), failed percutaneous transluminal coronary angioplasty requiring emergency coronary artery bypass grafting in 5, postoperative aortic valve replacement in 1, postoperative emergency coronary artery bypass grafting in 1, after cardiac transplantation in 1, and bridging to transplantation in 1. Mean blood pressure with PBY and IABP combined was 75 mm Hg versus 60 mm Hg with IABP off. Percutaneous cardiopulmonary bypass flows ranged from 0.8 to 2.1 L/min with a mean flow of 1.3 L/min. Time on IABP ranged from 24 hours to 1 week. Time on IABP to PBY ranged from 1 to 20 hours, and time on PBY ranged from 65 minutes to 20 hours. Ten of 16 (63%) were successfully weaned, and 3 died after weaning. Seven of 16 (44%) survive. Combined IABP with PBY appears to be a better therapy than either one individually. Staging the therapy as the balloon first in and last out appears to be a good methodology.

(Ann Thorac Surg 1992;54:908–10)

The intraaortic balloon pump [1–3] is the standard for mechanical support for low cardiac output syndromes. Other support modalities that have not achieved the popularity of the intraaortic balloon pump include Hemopump [4, 5], femoral-femoral bypass [6, 7], ventricular assist devices [6, 8], and percutaneous cardiopulmonary bypass [9]. In 1980 we described our initial experience with percutaneous intraaortic balloon pumping [10], and in 1983 we reported the initial experience with percutaneous cardiopulmonary bypass, first used in 1981 [11]. This review describes 16 patients who had both modalities of intraaortic balloon pumping and percutaneous cardiopulmonary bypass applied sequentially for the treatment of refractory cardiogenic shock. In this report we describe the beneficial affects of combining percutaneous intraaortic balloon pumping with percutaneous cardiopulmonary bypass.

Material and Methods

Between 1985 and 1989 16 patients had intraaortic balloon pumping combined with percutaneous cardiopulmonary bypass. The patient group consisted of 14 men and 2 women whose ages ranged from 29 to 72 years. Patients initially had a standard Percor (Datascope Corporation, Paramus, NJ) intraaortic balloon pump inserted, but because of continued low cardiac output percutaneous cardiopulmonary bypass was added. Timing was generally performed by electrocardiographic monitoring, but occasionally pressure timing was used. Balloon pumping was performed whenever possible with one to one timing with the heart rate. During episodes of rapid heart rate, timing was changed to two or three to one depending on which was most effective. The balloon was inserted before percutaneous bypass and removed last in patients who were weaned. Percutaneous bypass was initiated by percutaneous insertion into the femoral vessels of an 11F, 8-inch-long arterial cannula and two 11F 15-inch-long venous cannulas in which side holes were cut. A pediatric oxygenator was used in line initially, with a centrifugal pump (6 patients), and more recently, a roller pump (10 patients). All balloons and bypass cannulas were removed percutaneously.

The cause of cardiogenic shock in our patient population was acute myocardial infarction in 7 (5 anteroseptal, 2 inferior), failed percutaneous transluminal coronary angioplasty (4 left anterior descending, 1 right coronary artery + left anterior descending) in 5, postoperative aortic valve replacement in 1, postoperative emergency coronary artery bypass in 1, bridging to cardiac transplantation in 1, and after cardiac transplantation in 1. Hemodynamic data were recorded sequentially. Parameters recorded included free plasma hemoglobin along with standard laboratory evaluations. All patients received sodium heparin while on bypass to maintain the activated clotting time between 300 and 450 seconds. Monitoring of prothrombin time, platelets, fibrinogen, and fibrin degradation was done daily, or more frequently if abnormalities were noted. In most patients sequential two-dimensional

---

Accepted for publication March 3, 1992.

Address reprint requests to Dr Phillips, 411 Laurel, Suite 3250, Des Moines, IA 50314.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

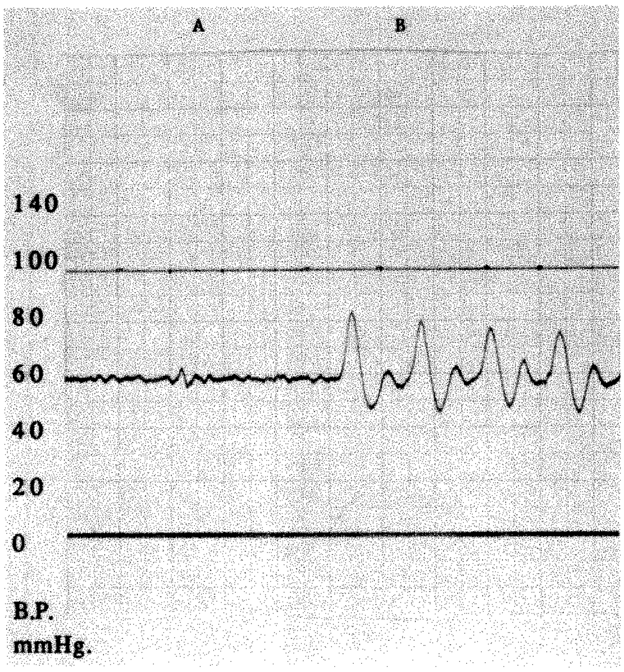


Fig 1. Intraaortic balloon pumping (B) *combined with percutaneous cardiopulmonary bypass* (A) *at a flow of 1.6 L/min. Note the increased pulse pressure with combined therapy.* (B.P. = *blood pressure.)*

echocardiograms were performed to assess progressive cardiac function.

Results

Time on the intraaortic balloon pump ranged from 24 hours to 1 week with a mean of 48 hours. Time from intraaortic balloon pump insertion to institution of percutaneous bypass ranged from 45 minutes to 20 hours with a mean of 12 hours. Percutaneous cardiopulmonary bypass flows ranged from 0.8 to 2.1 L/min with a mean flow of 1.3 L/min. Time on percutaneous bypass ranged from 65 minutes to 20 hours with a mean of 8 hours. Average mean blood pressure with the percutaneous bypass and intraaortic balloon pump combined was 75 mm Hg, as compared with 55 mm Hg (Fig 1) with the intraaortic balloon pump alone. Ejection fraction increased an average of 0.19 ± 0.07 in those weaned ($p > 0.01$) versus 0.07 ± 0.04 ($p < 0.5$) in nonweaned patients. The highest free plasma hemoglobin level was 650 g/L (9 hours percutaneous cardiopulmonary bypass + intraaortic balloon pump), with the average being 180 g/L. Appropriate corrections in coagulation deficiencies were made if clearly indicated, as long as the activated clotting time was between 300 and 450 seconds while on bypass. The use of the centrifugal pump was discontinued because of its inability to consistently perfuse against the resistance of the smaller arterial inflow cannula. With the centrifugal pump, periodic momentary decoupling of the pump head would occur. This was avoided with use of the roller pump without any detrimental effects.

Ten of the 16 patients (63%) were successfully weaned from the combined therapy. Three patients died later, 1 at 3 weeks after weaning of sepsis and 2 after transplantation (1 month and 3 months). Seven of the 16 patients (44%) are long-term survivors, from 4 months to 5 years.

Comment

Clinical devices for circulatory assistance have been available for almost 25 years [12–16], and new systems are being introduced frequently [4, 6, 9]. A support system that is simple and rapid to apply, is readily effective, and provides adequate support to a patient in cardiogenic shock is desirable. The intraaortic balloon pump, which has been used since its introduction in 1967 [1], fulfilled most of these criteria. A subgroup of patients who cannot be maintained with the intraaortic balloon pump alone need additional support. Percutaneous cardiopulmonary bypass, first used in 1981 and reported in 1983 [2], can support a patient in a low cardiac output state. Percutaneous bypass alone does not provide pulsatile flow or necessarily unload the left ventricle, or increase diastolic pressure (coronary perfusion pressure). Combining both modalities of intraaortic balloon pumping and percutaneous bypass fulfills the need for greater hemodynamic support and pulsatile flow during diastole, which increases coronary blood flow, and permits left ventricular systolic unloading. Lazar and associates [17] demonstrated experimentally the beneficial reduction of infarct size and reversal of hemodynamic deterioration with intraaortic balloon pumping and percutaneous cardiopulmonary bypass. The percutaneous application of these modalities allows them to be readily instituted in an emergency situation by individuals knowledgeable in vascular cannulation techniques.

Our 16 patients who remained in cardiogenic shock, in spite of intraaortic balloon pumping and cardiotonic drugs, probably would have died without further circulatory assistance. Percutaneous bypass supplied the added circulatory assistance and allowed 10 patients to be weaned from the combined therapy. Our mean cardiopulmonary bypass flow was 1.3 L/min. Although somewhat "low" by intraoperative cardiopulmonary bypass standards, the percutaneous cardiopulmonary bypass flow, combined with intraaortic balloon pumping and a beating heart, were adequate to sustain our patients. Thus, combining the patient's beating heart, intraaortic balloon pumping, and percutaneous cardiopulmonary bypass was additive. In no instance was it necessary to insert larger cannulas to achieve higher flow rates. This is advantageous, as it allowed us to provide support truly percutaneously (insertion and removal). Two of these patients, who underwent successfully transplantation but died of complications related to the transplant (1 mo, 3 mo), are considered survivors of the therapy. A third patient, who died after weaning, died at 3 weeks of complications of sepsis. Cardiac functional improvement was demonstrated by serial two-dimensional echocardiography in those 10 patients who were weaned. Seven patients remain alive at 4 months to 5 years.

Combined intraaortic balloon pumping and percutaneous bypass appears to be a better therapy than either one individually. Staging the therapy as the balloon first in and last out appears to be a good methodology. An additional application of this therapy is to support patients undergoing coronary artery "remodeling" or valvuloplasty in the catheterization laboratory. A newly designed multiple-lumen cannula has allowed easier application of intraaortic balloon pumping with percutaneous cardiopulmonary bypass in 6 additional patients.

References

1. Kantrowitz A, Tjonneland S, Freed PS, Phillips SJ, Butner AN, Sherman JL Jr. Initial clinical experience with intraaortic balloon pumping in cardiogenic shock. JAMA 1968;203:113–8.
2. Bregman D. Cardiac assist devices. In: Effler CD, ed. Blade's surgical disease of the chest. St. Louis: C.V. Mosby, 1978:773–5.
3. Subramanian VA, Paul J, Sos TA. Percutaneous intra-aortic balloon counter pulsation: a new technique. AAMI, 14th Annual Meeting, May 1978.
4. Frazier OH, Wampler RK, Duncan JM, et al. First human use of the Hemopump, a catheter-mounted ventricular assist device. Ann Thorac Surg 1990;49:299–304.
5. Phillips SJ, Barker L, Ballentine B, et al. Hemopump support for the failing heart. ASAIO Trans 1990;36:M629–32.
6. Pennington DG, Golding L, Hill JD, et al. Temporary mechanical support for cardiogenic shock. ASAIO Trans 1986;32:629–32.
7. Phillips SJ, Zeff RH, Wickemeyer WJ, et al. Bridging circulatory support before heart transplant without invasion of the mediastinum. J Heart Transplant 1987;6:116–9.
8. Phillips SJ, Kongtahworn C, Zeff RH, et al. A new left ventricular assist device: clinical experience in two patients. Med Instrum 1980;14:288–93.
9. Overlie PA. Emergency use of portable cardiopulmonary bypass. Cathet Cardiovasc Diagn 1990;20:27–31.
10. Phillips SJ, Gordon DF, Iannone L, et al. Clinical trial with a percutaneously inserted intra-aortic balloon pump: a wider spectrum of patient application. Thorac Cardiovasc Surg 1980;28:197–9.
11. Phillips SJ, Ballentine B, Slonine D, et al. Percutaneous initiation of cardiopulmonary bypass. Ann Thorac Surg 1983;36:223–5.
12. Kennedy JH. The role of assisted circulation in cardiac resuscitation. JAMA 1966;197:615–8.
13. Proctor E, Kowalik TA. Circulatory support by pump-oxygenator in experimental ventricular fibrillation and acute left heart failure induced by coronary artery ligation. Cardiovasc Res 1967;1:189–93.
14. Landé AJ, Edwards L, Bloch JH, et al. Clinical experience with emergency use of prolonged cardiopulmonary bypass with a membrane pump-oxygenator. Ann Thorac Surg 1970;10:409–23.
15. Evans D, Miyagishima RT, Tutassaura H, Ameli FM, Baird RJ. The effects of closed-chest venoarterial bypass with oxygenation on cardiopulmonary hemodynamics. J Thorac Cardiovasc Surg 1971;62:76–83.
16. Mattox KL, Beall AC Jr. Application of portable cardiopulmonary bypass to emergency instrumentation. Med Instrum 1977;11:347–9.
17. Lazar HL, Yang XM, Rivers S, Treanor P, Shemin RJ. Role of percutaneous bypass in reducing infarct size after revascularization for acute coronary insufficiency. Circulation 1991;84(Suppl):416–21.

Coronary Artery Bypass Using Internal Mammary Artery Branches

Jean E. Morin, MD, Giles Hedderich, MD, Normand L. Poirier, MD,
John Sampalis, PhD, and James F. Symes, MD

Cardiovascular and Thoracic Surgery Service, Department of Surgery, Royal Victoria Hospital, McGill University, Montreal, Quebec, Canada

The excellent long-term patency rates achieved with use of the internal mammary artery (IMA) to bypass the left anterior descending coronary artery have stimulated a variety of approaches to expand the use of this conduit in coronary bypass surgery. In this report we document our results using the two terminal branches of the IMA to bypass two arteries in a Y configuration. Sixty-seven patients received IMA Y grafts during a 6-month period in 1987. A total of 150 IMA branch anastomoses were performed (8 patients received bilateral IMA Y grafts). Fourteen of 67 patients were revascularized using IMA grafts only. Operative mortality was 2 of 67 (3%), and follow-up mortality was 5 of 67 (7.5%). Fifty-eight patients could be evaluated 37 ± 2.7 months later. Clinically 36% of patients reported some recurrence of angina and 12 of 47 (25%) had a positive electrocardiographic stress test. Four patients were reoperated on (2 redo coronary artery bypass grafting, 2 transplants). Sixty (40%) of the 150 branch anastomoses could be evaluated objectively and 30 (50%) were patent. Five (8.5%) were stenotic and 25 (41.5%) were occluded (overall patency rate, 58.5%). We conclude that although the use of IMA Y grafts is a technically feasible means to increase IMA usage, extended application of this technique cannot be recommended unless improved patency rates can be demonstrated.

(Ann Thorac Surg 1992;54:911–4)

From the experience of many centers, the internal mammary artery is considered the optimal conduit for coronary artery bypass grafts [1]. It has provided excellent long-term clinical results. Its patency rate is consistently reported to be greater than 90% after 10 years [2, 3]. It increases life span and improves cumulative event-free intervals [4]. The experience from many centers has shown an expected survival rate of 90% and freedom from ischemic manifestations of 77% at 5 years after myocardial revascularization [5]. Like other authors [6–10], we have attempted to expand the use of the internal mammary artery to achieve more extensive and complete revascularization.

The mammary artery can be used as a unilateral or bilateral conduit. It can be anastomosed end-to-side or sequentially or as a free graft. It has also been anastomosed in a retrograde fashion. Finally, its distal branches can be anastomosed separately to two different coronary arteries in a Y fashion.

Material and Methods

From the Royal Victoria Hospital cardiac surgery registry [11], we identified 67 patients who underwent mammary Y grafts during the first 6 months of 1987. The objective of this report is to describe the clinical outcome of these patients and the patency rate of the Y branches anastomosed to coronary arteries. All patients were operated on in a similar fashion. The mammary artery was dissected with a cautery to encompass a large, 2-cm-wide pedicle of soft tissue to prevent injury to the vessel or its branches. At the distal end the mammary artery divides into two major branches. One continues within the rectus muscle and the other gives a good-sized intercostal artery. Both branches were dissected for a distance of 2 to 3 cm. Once dissected, they were dilated with an infusion of papaverine chlorhydrate (Merck Frosst Canada Inc, Kirkland, Que, Canada), 65 mg into 200 mL of normal saline solution. Five to 10 mL of this solution was injected into one of the distal branches of the mammary artery through a small 16-gauge clear nylon epidural catheter (Concord/Portex, Keene, NH) threaded into the distal mammary artery (Fig 1).

The papaverine was contained within the mammary artery by blocking its exit with a Ligaclip (Ethicon Ltd, Peterborough, Canada) while cannulation for cardiopulmonary bypass was achieved. All anastomoses were made with continuous 7-0 Prolene (Ethicon Ltd). Myocardial protection was identical in all patients. An average of 1,713 ± 438 mL of cold crystalloid cardioplegia was delivered intermittently at 4°C. The average cross-clamp time was 61 ± 17 minutes, and the body temperature was lowered to an average of 27.5° ± 1.7°C.

Accepted for publication March 5, 1992.

Address reprint requests to Dr Morin, Royal Victoria Hospital, Suite S8.30, 687 Pine Ave West, Montreal, Que, H3A 1A1 Canada.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

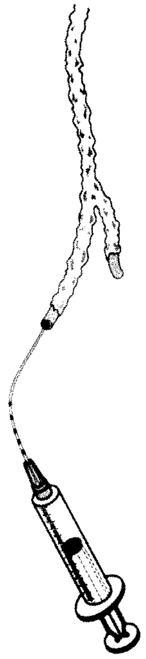


Fig 1. Papaverine is used to dilate the mammary artery.

The mammary branches were usually anastomosed to the left anterior descending artery and a diagonal artery, or to two different marginal arteries of the circumflex or the distal right coronary and its marginal branch (Fig 2).

Results

Sixty-seven patients were operated on. Two died in the immediate postoperative period for a mortality of 3%. Five other patients died during the next 3 years, 1 of cardiac disease and the other 4 of unrelated causes. Two patients could not be traced. Fifty-eight patients (87%) were evaluated at 37 ± 2.7 months after the operation.

Operations Performed

Fifty-nine patients underwent unilateral mammary Y anastomosis for a total of 118 anastomosed branches, and 8 received a bilateral mammary Y anastomosis for a total of 32 branches. Thus, a grand total of 150 mammary Y graft anastomoses were constructed. A total of 14 patients underwent revascularization using only the mammary arteries, whereas 53 had a combination of mammary and saphenous vein grafts.

Patients' Profile

The average age of the patients was 59 years; 87% of the patients were male. Six percent had a history of cerebrovascular disease, and 18% were diabetic. Thirty-six percent suffered from hypertension, and 49% had a previous myocardial infarction. Sixty-two percent had abnormal left ventricular function as evaluated by abnormal wall contraction on ventriculography. There was an average of 4 grafts constructed per patient.

Follow-up Evaluation

Fifty-eight patients were evaluated at an average of 37 ± 2.7 months after operation. Sixty-four percent were free of angina, and 36% had some degree of recurrent angina as defined by Campeau [12]. Six patients experienced some mild symptoms of congestive heart failure [13], and 2 had severe symptoms.

Forty-seven (81%) of the patients available for follow-up underwent an electrocardiographic stress test. Twenty-seven test results were negative, 8 inconclusive, and 12 positive. During the 3-year follow-up, 4 patients underwent reoperation, 2 for redo coronary bypass grafts and 2 for transplantation (Table 1).

Evaluation of Anastomoses

Of the 58 patients, 25 underwent recatheterization, and 1 heart could be inspected directly at time of transplantation. Thus, 45% of the cohort could be restudied by objective criteria. From a total of 150 branches anastomosed, 60 branches (40%) were assessed. Thirty branches (50%) were open with good flow (Fig 3), 5 (8%) had serious obstruction but were still patent, and 25 (42%) were occluded. Of all the branches studied, the anastomosis to the left anterior descending artery had the best patency rate (59%). However, this was not significantly different than the patency rates of other anastomosis sites ($\chi^2 = 6.70$; $p = 0.88$) (Table 2).

Comment

The cumulative experience of many centers shows an 83% chance of freedom from angina at 5 years after adequate myocardial revascularization. It is reported that 95% of internal mammary arteries that are anastomosed end-to-side to the left anterior descending artery are patent after

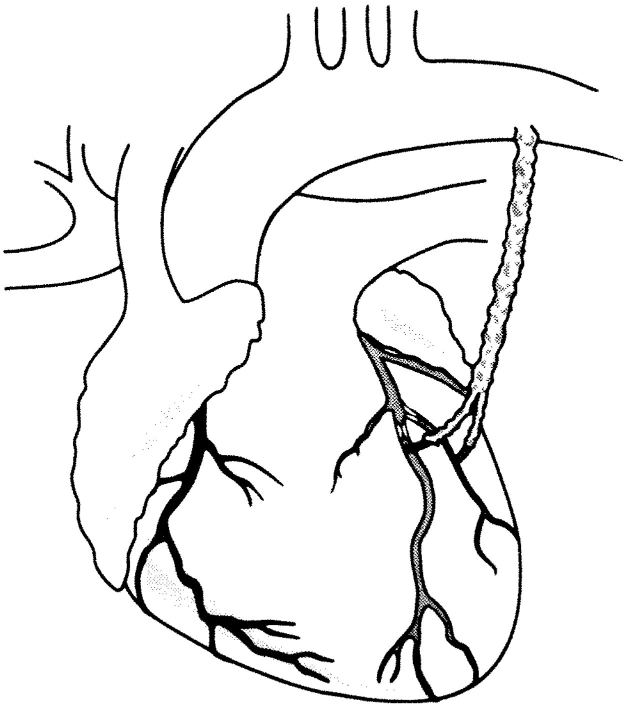


Fig 2. Mammary artery Y grafts to left anterior descending artery and diagonal artery.

10 years [14]. The use of the internal mammary artery in this fashion contributes to an increased longevity. The 10-year patency rate of the saphenous vein conduit is inferior to that of the internal mammary artery when anastomosed to the left anterior descending artery. The best reported rate at 10 years is approximately 80% [5]. Other large series report patency that ranges between 50% and 70% [15].

It is thus extremely important to try to maximize the patency rate of coronary artery bypass grafts by either extending the use of the mammary artery or finding other conduits that have a similar or even better patency rate.

Other authors, as well as ourselves, have tried to use the gastroepiploic artery, but the experience is limited and the long-term results are uncertain. In this cohort of patients we have tried to extend the use of the mammary artery by anastomosing its Y branches. This was successful in increasing our mean graft per patient from 3.4 to 4 grafts per patient. In addition 14 of 67 patients (21%) had complete revascularization with the mammary artery only, without the use of saphenous veins.

The operative mortality of 3% is the same as reported for large series of patients. On the other hand, a recurrent rate of angina of 36% at 37 months is higher than reported in cumulative experiences by many centers [5]. On clinical grounds, therefore, it appears that mammary Y grafts are not as satisfactory as direct mammary anastomosis to the left anterior descending artery combined with use of the saphenous vein. Four of 67 patients (6%) underwent reoperation within 3 years, which is higher than the usual reoperation rate of 10% at 10 years.

Of the 150 Y branches that were originally constructed, 60 branches were evaluated. Although the patients who accepted recatheterization were in general more symptomatic than the patients who refused the test, a 42% rate of occlusion in this group is relatively high for the mammary artery conduit.

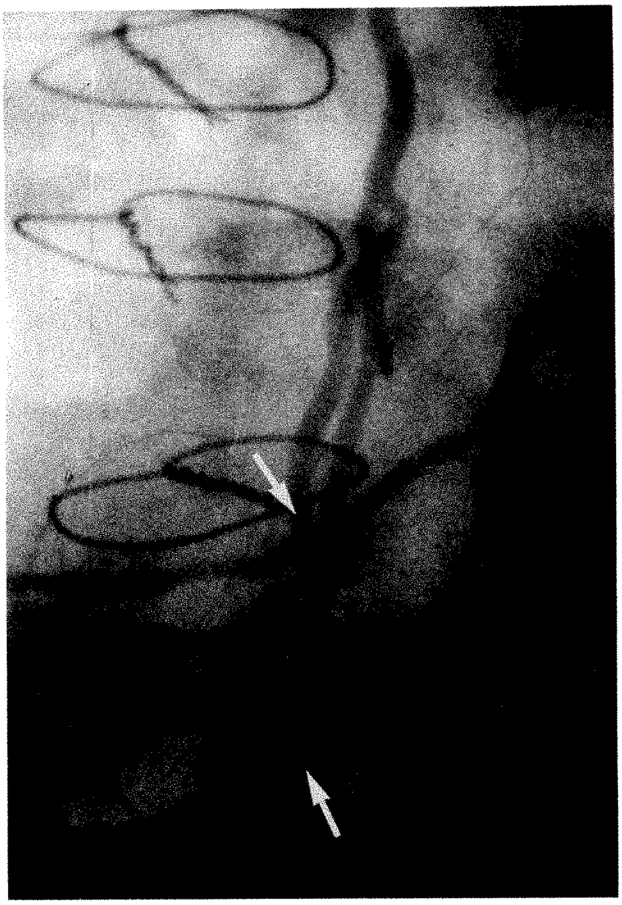


Fig 3. Angiogram of mammary artery Y grafts (arrows) *to two marginal branches of circumflex artery.*

Table 1. Follow-up Evaluation[a]

Variable	No. of Patients	Percent
Angina		
0	37	64
1	11	19
2	4	7
3	4	7
4	2	3
CHF		
Mild	6	10
Severe	2	3
Stress test		
Negative	27	46
Inconclusive	8	14
Positive	12	21
Not done	11	19
Reoperation		
Redo CABG	2	
Transplantation	2	

[a] Fifty-eight patients were followed up 37 ± 2.7 months (mean ± standard deviation) after operation.

CABG = coronary artery bypass grafting; CHF = congestive heart failure.

Of the 150 grafts, if we assume that only these 25 studied grafts are blocked and that all the others are open, it would still mean that the occlusion rate is 17%. Thus, our real occlusion rate is situated between 17% and 42%, which is higher than usually reported for this conduit when used as a single pedicle graft. Fourteen patients received Y grafts only, and 10 of 14 (71%) were asymptomatic at the time of reevaluation. Ten branches in 5 patients of this cohort were evaluated by angiography. Four were open, two partially open, and four closed. This is a very small subgroup of patients, and it is not justified to draw a very definitive conclusion. Nevertheless, their clinical status and angiographic results are the same as for the rest of the group.

Although we can only speculate as to the reasons for the high occlusion rate, it was our impression that this type of anastomosis is technically more difficult than the standard mammary artery to left anterior descending artery anastomosis. The Y branches are of smaller diameter and could in general only accept the 16-gauge epidural catheter at the time of dilation. The vessel wall

Table 2. Branches Anastomosed

Graft Location	No. of Branches	Patency		
		Condition	No.	Percent
LAD	22	Open	13	59
		Partially closed	2	9
		Closed	7	32
First DG	16	Open	6	37
		Partially closed	2	12
		Closed	8	50
Second DG	6	Open	3	50
		Partially closed	1	17
		Closed	2	33
First OM	7	Open	4	57
		Partially closed	0	
		Closed	3	43
Second OM	7	Open	3	43
		Partially closed	0	
		Closed	4	57
PVB	1	Open	1	
		Partially closed	0	
		Closed	0	
PDA	1	Open	0	
		Partially closed	0	
		Closed	1	

DG = diagonal artery; LAD = left anterior descending artery; OM = obtuse marginal branch; PDA = posterior descending artery; PVB = posterior ventricular branch.

appeared thinner and more friable, and its layers seemed to separate more easily.

In addition, the coronary artery anatomy is not always suitable for the Y grafts to fit perfectly. This can lead to slight angulations and increased tension on the limbs of the Y grafts, which may contribute to the higher obstruction rate.

All anastomoses were constructed using 2.5× or 3.5× magnifying loupes and continuous 7-0 Prolene suture. It is possible that better results could be obtained with interrupted techniques using finer suture material with an operating microscope.

In conclusion, this study demonstrates the technical feasibility of using mammary artery Y grafts for multiple coronary bypass procedures. Its use is limited, however, by the coronary anatomy and the small sizes of the Y branches. The use of the Y branches of the mammary should be considered when conventional mammary or vein conduits cannot be used in the classic way. We believe that this technique should be part of the cardiac surgeon's armamentarium, but its use should be limited unless further refinements in surgical technique can be demonstrated to improve patency.

We thank Ms Nadine Fosset, RN, for tracing patients for follow-up, and data gathering.

References

1. Loop FD, Lytle BW, Cosgrove DM. New arteries for old. Circulation 1989;79(Suppl 1):40–5.
2. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary-artery-graft on 10-year survival and other cardiac events. N Engl J Med 1986;314:1–6.
3. Tector AJ, Schmahl TM, Canino VR, Kallies JR, Sanfilippo D. The role of the sequential internal mammary artery graft in coronary surgery. Circulation 1984;70(Suppl 1):222.
4. Cameron A, Kemp HG Jr, Green GE. Bypass surgery with the internal mammary artery graft: 15 year follow-up. Circulation 1986;74(Suppl 3):30–6.
5. Kirklin JW, Naftel DC, Blackstone EH, Pohost GM. Summary of a consensus concerning death and ischemic events after coronary artery bypass grafting. Circulation 1989;79(Suppl 1):81–91.
6. Slater AD, Gott JP, Gray LA Jr. Extended use of bilateral internal mammary arteries for coronary artery disease. Ann Thorac Surg 1990;49:1014–5.
7. Kieser TM, FitzGibbon GM, Keon WJ. Sequential coronary bypass grafts. J Thorac Cardiovasc Surg 1986;91:767–72.
8. Landymore RW, Chapman DM. Anatomical studies to support the expanded use of the internal mammary artery graft for myocardial revascularization. Ann Thorac Surg 1987;44:4–6.
9. Tector AJ. Fifteen years' experience with the internal mammary artery graft. Ann Thorac Surg 1986;42(Suppl):S22–7.
10. Singh RN, Sosa JA. Internal mammary artery-coronary anastomosis. Influence of the side branches on surgical result. J Thorac Cardiovasc Surg 1981;82:909–14.
11. Morin JE, Symes JF, Ralphs-Thibodeau S, Tasse S, Morin A, Lefebvre C. A microcomputer system for the practising cardiac surgeon. Can J Surg 1981;29:364–6.
12. Campeau L. Grading of angina pectoris. Circulation 1976;54:522–3.
13. Austen WG, Edwards JE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease. Circulation 1975;51:7–40.
14. Kirklin JW, Akins CW, Blackstone EH, et al. ACC/AHA guidelines and indications for coronary artery bypass graft surgery. Circulation 1991;83:1125–73.
15. Campeau L, Enjalbert M, Lespérance J, Vaislic C, Grondin CM, Bourassa MG. Atherosclerosis and late closure of aortocoronary saphenous vein grafts: sequential angiographic studies at 2 weeks, 1 year, 5 to 7 years, and 10 to 12 years after surgery. Circulation 1983;68(Suppl 2):1–7.

Isolated Biventricular Working Rat Heart Preparation

Todd L. Demmy, MD, George J. Magovern, MD, and Race L. Kao, PhD

Division of Thoracic Surgery, Department of Surgery, Allegheny Campus of the Medical College of Pennsylvania, and
Allegheny-Singer Research Institute, Pittsburgh, Pennsylvania

The isolated perfused heart from small animals has been used extensively for hemodynamic and metabolic studies. The left working heart preparation proved superior to the Langendorff model for functional evaluations but has not allowed study of right heart function. A simple and inexpensive biventricular working heart preparation has been developed by modifying the left working rat heart model. Under general anesthesia the heart was removed surgically leaving sufficient vessels attached to it. Cannulation of the aorta, left atrium, right atrium, and pulmonary artery was completed in 10 minutes. A pressurized compliance chamber allowed rapid and reliable regulation of aortic impedance. For the 7 hearts that were subjected to 3-hour biventricular perfusion (their end points expressed as percent of their initial values), the aortic output (95% ± 3%), pulmonary flow (88% ± 9%), mean aortic pressure (109% ± 5%), mean pulmonary pressure (100% ± 2%), heart rate (106% ± 8%), myocardial adenosine triphosphate level (85% ± 8%), and creatine phosphate level (89% ± 4%) were all maintained at physiologic levels. For the 11 hearts that were converted from left working heart preparation to biventricular working mode, significant improvement in stroke volume, aortic and cardiac output, and pressure development were observed. Experimental results indicate that the biventricular working model for isolated perfused rat hearts is superior to the left working preparation for studying the function of the total heart. Further study of the biventricular perfused working rat heart appears warranted.

(Ann Thorac Surg 1992;54:915–20)

Seventy-two years after the first successful perfusion of isolated hearts by Langendorff [1] in 1895, a major improvement was achieved by Neely and associates [2]. They developed the left-side working heart. This isolated perfused left working heart has been used extensively for studying the effects of ischemia, anoxia, hormones, drugs, and substrates on the metabolic and mechanical functions of the heart [3, 4]. Establishment of a left-side working heart has allowed the assessment of left ventricular function by varying preload (left atrial pressure), afterload (aortic pressure or impedance), and metabolic activities. Unfortunately, the preparation is not suitable for studying right heart function. In addition, when only the left side of the heart is actively pumping, imperfect evaluations due to ventricular septal shifting and an inactive right heart are observed. The purpose of this study was to develop a simple and inexpensive biventricular working heart preparation.

Material and Methods

Animals

Forty-nine male Sprague-Dawley rats weighing 350 to 400 g were obtained from a local licensed vendor. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). After overnight fasting, the animals were heparinized (sodium heparin, 2.5 mg) and anesthetized (chloral hydrate, 36 mg/100 g body weight) by intraperitoneal administration. The thorax was opened, and the heart was removed. The isolated heart was dropped into a beaker of cold perfusate (2°C) before being used for the experimental study. Fifteen rats were used for the establishment of the model, and 34 rats were used for evaluation of the preparation.

Perfusion Apparatus for Biventricular Working Hearts

The left-side working heart model previously published [5, 6] was modified to develop the biventricular working preparation (Fig 1). The apparatus consists of 7 major parts: (1) cannula assembly, (2) compliance chamber, (3) pulmonary outflow, (4) venous oxygenation reservoirs, (5) heart chamber, (6) recirculation reservoir with filter, and (7) peristaltic pump. The cannula assembly (Fig 2, top) was modified from that in an earlier report [6] to accommodate the flexible pulmonary artery and right atrial (90-degree angle) cannulas. The compliance chamber, which provides a dynamic impedance against the aortic output, is a major improvement as compared with other reported models. Rapid and reliable changes in afterload are possible by adjusting air pressure within the compliance chamber (Fig 1, *E*; Fig 2, bottom). The chamber was constructed of a 16-cm-long, 4-cm-diameter Pyrex glass tube sealed by rubber stoppers (No. 8). Each stopper was penetrated through the center by a stainless steel tube (3.2 mm diameter; Small Parts, Inc, Miami, FL), and

---

Accepted for publication March 5, 1992.

Address reprint requests to Dr Kao, Department of Surgery, East Tennessee State University, Box 70575, Johnson City, TN 37614-0575.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

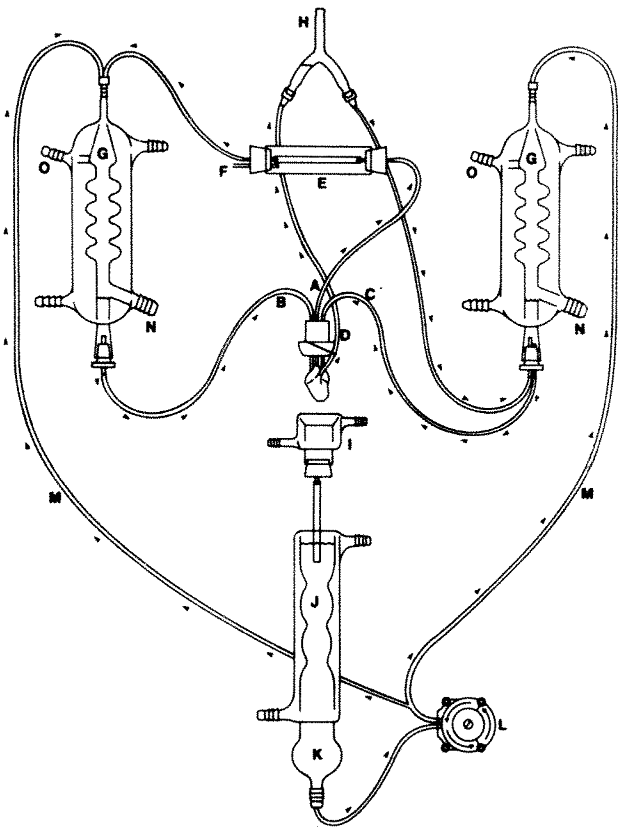


Fig 1. Diagram of biventricular working heart apparatus. (A = aortic cannula; B = right atrial cannula; C = left atrial cannula; D = pulmonary artery cannula; E = compliance chamber; F = air infusion port; G = venous oxygenation reservoirs; H = pulmonary outflow; I = heart chamber; J = recirculation reservoir; K = filter; L = peristaltic pump; M = recirculation lines; N = overflow to recirculation reservoir; O = oxygen port.) Unmarked ports connect to thermally regulated circulating water bath.

these stainless steel tubes were connected by very thin-walled latex tubing (3.5 mm diameter, custom dipped). Another stainless steel tube was passed through one of the rubber stoppers and was used to adjust and monitor the intra chamber pressure (Fig 1, *F;* Fig 2, *F*).

The height of pulmonary outflow and venous oxygenation reservoirs was adjusted independently to produce the desired pulmonary resistance and venous pressures. All the reservoirs were water jacketed to be maintained at 37°C, and the buffer was continuously equilibrated with 95% O_2 and 5% CO_2. Preliminary retrograde perfusion and the recording of aortic pressure were accomplished through a side arm of the aortic cannula. Pulmonary artery pressure was measured through a side port of the pulmonary artery cannula. The cannula assembly with the heart was fitted into the water-jacketed heart chamber to maintain the heart at the selected temperature during biventricular perfusion.

Isolation and Perfusion of the Heart

Under general anesthesia, a transverse upper abdominal incision was made. After bilateral anterolateral thoracotomy, retraction and inversion of the anterior chest wall was achieved. The heart was isolated with sufficient vessels attached to it and placed in a beaker of cold perfusate (2°C) to stop its activity. After aortic cannulation, a 15-minute period of preliminary retrograde perfusion at a perfusion pressure of 60 mm Hg was begun without recirculation. Krebs-Henseleit bicarbonate buffer at 37°C equilibrated with 95% O_2 and 5% CO_2 containing normal plasma levels of amino acids [7], 15 mmol/L glucose, and 400 μU/mL insulin was used. During preliminary perfusion, the excessive tissue was trimmed, and the left atrium (through pulmonary vein), right atrium (through inferior vena cava), and pulmonary artery were cannulated in sequence.

The pulmonary artery cannula was flexible and freely movable to facilitate aortic and left atrial cannulation. A 4-0 silk ligature was passed around the distal portion of the pulmonary artery before the cannula was inserted. An elastic rubber band provided pulmonary artery cannula retractability during initial cannulation and stability during pulmonary artery cannulation. The pulmonary artery cannula was secured by the silk ligature without compromising the pulmonary valve and was tied to the aortic cannula to prevent distortion of the cardiac infundibulum. After cannulation of the heart, biventricular perfusion was started by clamping the retrograde perfusion inflow and opening the inflow tubing connected to the cannulas.

Measurements of Cardiac Hemodynamics and Metabolism

Atrial, pulmonary artery, aortic, and compliance chamber pressures were measured simultaneously using 1290C universal quartz pressure transducers (Hewlett Packard, Andover, MA) and recorded with a multichannel chart recorder (Western Graphtec, Irvine, CA). The pressure tracing was also used to determine the heart rate while the chart recorder was turned to a calibrated high speed.

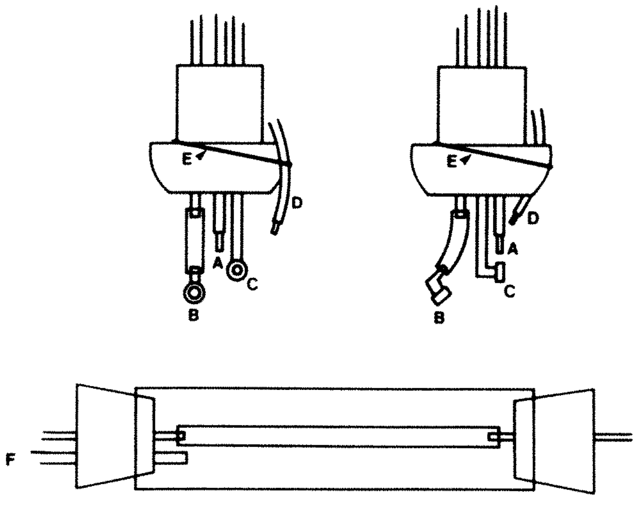


Fig 2. Anterior and lateral views of cannula mount and closer view of compliance chamber. (A = aortic cannula; B = right atrial cannula; C = left atrial cannula; D = pulmonary artery cannula; E = elastic band; F = air infusion port for pressure adjustment and monitoring.)

Aortic output and pulmonary flow (PF) were measured by the timed collection of the outflow tracts. Coronary flow was collected from the pulmonary artery outflow while the right atrial inflow was temporarily interrupted.

The mean arterial pressure (MAP) and mean pulmonary artery pressure (MPAP) were calculated by: ⅓ (systolic pressure + 2 · diastolic pressure). Developed pressure was used to indicate the difference between arterial systolic and diastolic pressures. Cardiac output (CO) was the sum of aortic output and coronary flow. Stroke volume was obtained by dividing the CO by the heart rate (HR). The arterial resistance (AR) and pulmonary resistance (PR) were estimated by the following formulas:

$$AR = (MAP - \text{right atrial pressure}) \cdot 79.9/CO.$$

$$PR = (MPAP - \text{left atrial pressure}) \cdot 79.9/PF.$$

The left ventricular stroke work index (LVSWI) and right ventricular stroke work index (RVSWI) were calculated by the following equations:

$$LVSWI = (MAP \cdot CO \cdot 14.4)/(HR \cdot \text{body surface area}).$$

$$RVSWI = (MPAP \cdot PF \cdot 14.4)/(HR \cdot \text{body surface area}).$$

At a predetermined time under proper perfusion, each heart was frozen with Wollenberger tongs that had been cooled to the temperature of liquid nitrogen. The frozen heart pellets were pulverized before being extracted with 6% perchloric acid (0°C). A portion of the pulverized powder was used to determine tissue water content and percent dry weight by the published method [6]. After centrifugation the supernatant was neutralized and filtered (0.2 μm) before adenosine triphosphate, adenosine diphosphate, adenosine monophosphate, creatine phosphate, and creatine content were determined using a high-performance liquid chromatography system (Waters Co, Milford, MA) with the method published previously [8]. The neutralized tissue extracts were used for enzymatic determination of lactate content [9]. The pellet was subjected to alkaline digestion before samples were taken for protein [10] and glycogen [11] measurements.

Statistical Analysis

Values were expressed as mean ± standard error of the mean. The changes in hemodynamic performance of the hearts during biventricular working versus left-side working and during the 3 hours of biventricular working were compared by paired *t* test. For comparison of sample means, analysis of variance with one-way classification [12] was used. A value of p less than 0.05 was considered statistically significant.

Results

The average cannulation time for the 34 biventricular working rat hearts was 10 minutes. The MAP and AR were closely regulated by the compliance chamber pressure in a linear relationship (Fig 3). The correlation coefficients for aortic pressure (0.73) and AR (0.78) were statistically significant ($p < 0.01$). Based on this work, 80 mm Hg compliance chamber pressure, 15 mm Hg PR, and 9.4 mm Hg atrial pressures were selected for the subsequent studies.

When 7 rat hearts were subjected to biventricular perfusion for 3 hours, the hemodynamic performance remained stable for the entire experimental duration. At the end of the 3-hour perfusion period, the aortic output (95% ± 3%), PF (88% ± 9%), MAP (109% ± 5%), MPAP (100% ± 2%), and HR (106% ± 8%) were all well maintained as compared with their initial values (Table 1). When three groups of hearts were frozen, one at the beginning (n = 6), one at 1 hour (n = 6), and one at 3 hours (n = 7) of biventricular perfusion, their energy metabolism was stable at physiologic levels (Table 2). The slight but insignificant decrease in creatine phosphate level after prolonged perfusion was most likely due to the minute increase in myocardial lactate. The total creatine (creatine phosphate + creatine) and adenine nucleotides content of the heart decreased about 15% after 3 hours of biventricular working. A statistically insignificant decrease in myocardial glycogen was observed at 3 hours of in vitro biventricular working.

For a group of 11 hearts that were started as left ventricular working preparation, converted to biventricular working mode, and then returned to left heart working mode, the changes in hemodynamic performance are summarized by Table 3. The data obtained after biventricular cannulation but before opening the right atrial inflow were considered as biventricular working stage I. Significant increases in stroke volume, aortic and cardiac output, pressure development, and LVSWI were found during biventricular working stage I and II (see Table 3). Significant increases in aortic systolic pressure and developed pressure were observed only during biventricular working stage I. The PF is close to the CO while both ventricles are actively pumping (biventricular working stage II). A small leakage collected from the cardiac surface was persistent under the condition of biventricular working stage II. The leakage was 4.2 ± 0.6 mL/min, which represented about 6% of the CO.

The percent dry weight (18%) and tissue water content (4.50 g H_2O/g dry heart) did not change for up to 3 hours of perfusion. The samples used for this study (pulverized frozen heart powder) tend to overestimate the tissue water content and underestimate the percent dry weight. When hearts are freeze-clamped during active working and proper perfusion, it is impossible to avoid a portion of the perfusate being frozen with the heart pellet. However, intramyocardial edema seems not to be a concern for this study due to unchanged percent dry weight and tissue water content.

Comment

Early experience with this isolated biventricular working heart model has been promising for several reasons. A compliance chamber, instead of a static fluid column,

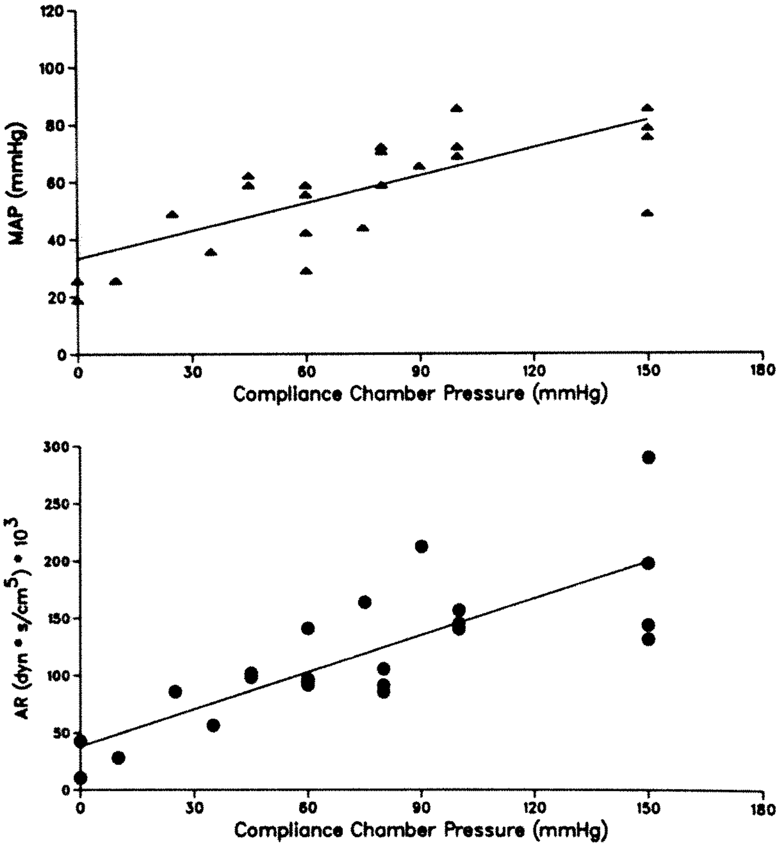


Fig 3. Effect of regulation of compliance chamber pressure on mean aortic pressure (MAP, top) and arterial resistance (AR, bottom).

provides aortic output impedance by simulating a vascular bed. This is closer to the physiologic conditions for the left ventricle because the compliance chamber can better accommodate a pulsatile output. A similar chamber could be constructed easily for right ventricular output; however, a static fluid column was chosen because less resistance is required in the pulmonary circulation. This model also functioned well because it was built upon the

Table 1. Stability of Hemodynamic Performance for the Biventricular Working Hearts[a]

Hemodynamic Parameters	Biventricular Perfusion Time (min) 10	30	60	120	180
Aortic output (mL/min)	35 ± 1	35 ± 1	34 ± 1	35 ± 1	33 ± 1
Coronary flow (mL/min)	25 ± 2	25 ± 2	24 ± 1	24 ± 1	22 ± 2
Cardiac output (mL/min)	60 ± 3	60 ± 2	59 ± 2	59 ± 2	55 ± 3
Pulmonary flow (mL/min)	56 ± 3	62 ± 6	58 ± 5	55 ± 4	49 ± 5
Heart rate (beats/min)	231 ± 16	225 ± 26	252 ± 17	246 ± 15	246 ± 18
Stroke volume (mL/beat)	0.29 ± 0.03	0.27 ± 0.02	0.24 ± 0.02	0.24 ± 0.01	0.23 ± 0.02
Mean aortic pressure (mm Hg)	73 ± 4	77 ± 3	80 ± 2	78 ± 2	80 ± 3
Mean pulmonary artery pressure (mm Hg)	16 ± 1	16 ± 1	16 ± 1	16 ± 1	16 ± 1
Arterial resistance ([dyn · s/cm^5] × 10^3)	87.8 ± 5.6	93.1 ± 5.0	99.2 ± 3.2	95.7 ± 4.4	107.5 ± 5.1[b]
Pulmonary resistance ([dyn · s/cm^5] × 10^3)	11.4 ± 0.7	11.1 ± 0.8	11.9 ± 0.8	13.0 ± 0.8	13.3 ± 1.1
LV stroke work index (g · m/beat · m^2)	5.6 ± 0.7	5.3 ± 0.4	5.0 ± 0.5	5.0 ± 0.3	4.9 ± 0.5
RV stroke work index (g · m/beat · m^2)	1.1 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	0.9 ± 0.1	0.8 ± 0.1[b]

[a] The definitions of hemodynamic parameters are given in the Material and Methods section. A group of 7 hearts was used for this study.

[b] $p < 0.05$ compared with the values obtained at 10 minutes of biventricular perfusion.

LV = left ventricular; RV = right ventricular.

Table 2. Stability of Metabolic Activities for the Biventricular Working Hearts

Metabolic Parameters[a]	Biventricular Perfusion Time (min)[b]		
	10	60	180
ATP	35.6 ± 1.4	33.7 ± 1.0	30.2 ± 2.7
ADP	12.8 ± 0.6	13.1 ± 1.2	10.5 ± 0.6[c]
AMP	1.4 ± 0.2	2.3 ± 0.6	1.8 ± 0.1
CP	80.6 ± 3.7	70.6 ± 6.8	71.5 ± 4.9
C	63.2 ± 1.6	56.4 ± 3.8	51.9 ± 2.8[c]
Lactate	6.8 ± 1.0	9.0 ± 2.2	10.0 ± 1.8
Glycogen	108 ± 12	105 ± 8	76 ± 10

[a] The myocardial levels of adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP), creatine phosphate (CP), creatine (C), and lactate are given as mean ± standard error of the mean in μmol/g heart protein. The data for glycogen are expressed in μmol glucose equivalent/g heart protein. [b] For the 10-minute and 60-minute biventricular perfusion groups, 6 hearts per group were used. Seven hearts were obtained for the 180-minute perfused group. [c] $p < 0.05$ compared with the 10-minute group.

left working heart model, which has considerable refinement. In addition, most institutions could construct this apparatus with few additional expenditures. Other than the cost for hardware, this model could be established easily by investigators who have experience with left working heart preparations. Because aortic and left atrial cannulation procedures are essentially the same as the classic model, an experienced investigator would need only to learn procedures for right atrial and pulmonary artery cannulation. Therefore, this simple and inexpensive biventricular working heart preparation should be easily reproducible.

We believe that cannulation has been the "Achille's heel" of similar studies [13] and that the described cannulation technique may be the most important part of the preparation. If a different technique is to be used, several of the following recommendations should be helpful. The cannula mount should be built away from the rest of the apparatus to allow the experimenter a near-360-degree view of the heart once it is secured to the aortic cannula. The heart should be oriented so that the pulmonary vein and the coronary sinus are toward the experimenter. The pulmonary artery should be prepared for cannulation before cannulation of the left atrium to prevent subsequent impaired exposure. The pulmonary artery and right atrial cannulas should be flexible. This allows retraction to aid exposure during the early steps of cannulation. It also allows for conformation to the particular anatomy of the individual hearts. Once inserted, the pulmonary artery cannula can be tied to the aortic cannula, and the right atrial line can be fixed to the rigid left atrial cannula. This is important because it prevents the flexible cannulas from shifting after being properly positioned. Without such fixation, the aortopulmonary anatomy would become distorted, the coronary sinus would be compressed, or the atrial tissue could tear. The cannulation techniques described in this study assure the success of the biventricular working heart.

Once cannulation is complete, this preparation has other positive features. The working heart can be switched from a univentricular to a biventricular preparation simply by occluding the right atrial inflow and supporting the left atrial inflow with the pump. In univentricular mode, the PF is equal to the coronary flow. This is a more physiologic way to measure flow because the coronary sinus is not open to atmospheric pressure (as it is in the Langendorff and left working heart models). In addition, it has been difficult to distinguish between leakage and coronary flow in the isolated left working heart. This preparation allows the distinction. The hearts tested in this model have shown some obligate leak into the heart chamber, which has persisted despite improvements in the cannulation technique. This flow was about 6% of the CO and probably represents flow through the cut surfaces of the excised heart and transudation. This flow remained stable and did not affect cardiac functions. The biventricular working heart provided more reliable measurements in coronary flow and samples for metabolic studies.

This apparatus was able to run for up to 1 hour without the peristaltic pump that is needed in the other working models. This was achieved because it was unnecessary to return coronary flow back to the circuit (because coronary

Table 3. Comparison of Left Working and Biventricular Working Hearts[a]

Hemodynamic Parameters	Left Working	Biventricular Working Stage I	Biventricular Working Stage II
Aortic output (mL/min)	34 ± 1	40 ± 2[b]	39 ± 1[b]
Coronary flow (mL/min)	24 ± 1	23 ± 1	24 ± 1
Cardiac output (mL/min)	58 ± 2	63 ± 2[b]	63 ± 2[b]
Pulmonary flow (mL/min)	24 ± 1	23 ± 1	57 ± 3[c]
Heart rate (beats/min)	239 ± 8	203 ± 13	200 ± 16
Stroke volume (mL/beat)	0.25 ± 0.01	0.32 ± 0.03[b]	0.35 ± 0.02[b]
Compliance chamber pressure (mm Hg)	82 ± 1	83 ± 1	84 ± 1
Aortic systolic pressure (mm Hg)	134 ± 3	151 ± 4[b]	144 ± 2
Aortic diastolic pressure (mm Hg)	38 ± 2	31 ± 2	38 ± 3
Developed pressure (mm Hg)	96 ± 4	120 ± 4[c]	106 ± 4
Arterial resistance ([dyn · s/cm^5] × 10^3)	97.8 ± 4.3	90.2 ± 2.9	83.1 ± 2.1[b]
LV stroke work index (g · m/beat · m^2)	4.6 ± 0.02	6.2 ± 0.5[b]	6.4 ± 0.4[c]

[a] Hemodynamic parameters are defined in the Material and Methods section. Stages are defined as follows: left working—aortic and left atrial cannulation completed and left ventricle actively pumping; biventricular working stage I—biventricular cannulation completed and left ventricle actively pumping with right atrial inflow clamped; biventricular working stage II—biventricular cannulation completed and both left and right ventricles actively pumping. Eleven hearts were started as left ventricular working preparation, converted to biventricular working, and then returned to left heart working mode. The initial and final hemodynamic parameters during left heart working were not different for the same heart; the combined data are presented in this table. [b] $p < 0.05$ and [c] $p < 0.01$ compared with left working condition.

LV = left ventricular.

flow never left the circuit). The pump was needed to prime the system and return epicardial flow back to the circuit, although this could have been done manually. This mode of operation did require careful observation of the balance between right and left heart flow and connection of the venous reservoirs. This preparation is highly desirable for experiments that require small volumes (<50 mL) of circulating buffer such as in substrate utilization or expensive pharmacologic studies.

Although the myocardial adenosine triphosphate and creatine phosphate content were maintained after 3 hours of biventricular working, the level of total creatine and adenine nucleotides decreased about 15%. Supplementing the perfusate with the proper amount of adenosine, adenine nucleotide, and creatine phosphate should prevent this [14–19]. Because the volume of perfusate required for the biventricular working heart preparation is relatively small (<50 mL), replacing it with fresh perfusate or supplying additional glucose could eliminate the insignificant decrease of glycogen at 3 hours of continuous working.

There were few publications with which to compare the biventricular working heart model. Liu [13] reported a guinea pig model in 1986, which was probably the first biventricular working model; however, it has not been reproduced or widely accepted. His preparation required an elaborate harvest of the heart using microsurgical technique in a ventilated animal and cannulation of the coronary sinus. Although he reported 5-hour durability, this was with an aortic pressure of 35 mm Hg, very low rate of change of pressure, and no data reporting trends over time. The apparatus required electromagnetic flow transducers and amplifiers and did not have an aortic compliance chamber. Despite these problems, his study did show that the right heart provided up to 25% of the total cardiac work and up to half of the left ventricular contractility [13].

The biventricular working rat heart preparation would appear to be durable and inexpensive. It has the potential of being a powerful tool in directly assessing right heart function after treatment with various pharmacologic agents. Right heart recovery after ischemia, cardioplegia, or organ preservation could then be measured without the need for a cumbersome, large animal model. The contribution of right ventricular work to lipid, carbohydrate, protein, and other substrate utilization could be attained easily by repeating those experiments that were designed originally for the isolated left working heart. Finally, the left heart functions in this model without the deleterious effects of septal shift caused by nonfunctioning of the right ventricle. The left heart also has a more physiologic outflow impedance. Further study of this promising model appears warranted, especially when both left and right ventricular functions are of interest.

We thank M. Snyder for his technical assistance, B. Bonfiglio for helping prepare the manuscript, and Dr R. E. Clark for his valuable advice.

References

1. Langendorff O. Untersuchungen am uberlebenden Saugethierherzen. Pflugers Arch Ges Physiol Mensch Tiere 1895;61: 291–332.
2. Neely JR, Liebermeister H, Battersby EJ, Morgan HE. Effect of pressure development on oxygen consumption by isolated rat heart. Am J Physiol 1967;212:804–14.
3. Morgan HE, Siehl DL. Perfused working rat heart for metabolic studies. In: Larner J, Pohl S, eds. Methods in diabetes research. New York: Wiley, 1984:211.
4. Williamson JR, Kobayashi K. Use of the perfused rat heart to study cardiac metabolism: retrospective and prospective views. Basic Res Cardiol 1984;79:283–91.
5. Morgan HE, Chua BHL, Fuller EO, Siehl D. Regulation of protein synthesis and degradation during in vitro cardiac work. Am J Physiol 1980;238:E431–42.
6. Kao RL, Conti VR, Williams EH. Effect of temperature during potassium arrest on myocardial metabolism and function. J Thorac Cardiovasc Surg 1982;84:243–9.
7. Rannels DE, Kao RL, Morgan HE. Effect of insulin on protein turnover in heart muscle. J Biol Chem 1975;250:1694–701.
8. Kao RL, Trumble DR, Magovern JA, Christlieb IY, Magovern GJ. Fatigue resistant muscle with preserved force and mass for cardiac assist. J Card Surg 1991;6(Suppl 1):210–7.
9. Marbach EP, Weil MH. Rapid enzymatic measurement of blood lactate and pyruvate. Clin Chem 1967;13:314–25.
10. Smith PK, Krohn RI, Hermanson GT, et al. Measurement of protein using bicinchoninic acid. Anal Biochem 1985;150: 76–85.
11. Walaas O, Walaas E. Effect of epinephrine on rat diaphragm. J Biol Chem 1950;187:769–76.
12. Steel RGD, Torrie JH. Principles and procedures of statistics. New York: McGraw-Hill, 1960.
13. Liu CT. Techniques for isolation and performance of the perfused guinea pig working heart. Am J Vet Res 1986;47: 1032–43.
14. Kao RL, Magovern GJ. Prevention of reperfusional damage from ischemic myocardium. J Thorac Cardiovasc Surg 1986; 91:106–14.
15. Bolling SF, Bies LE, Bove EL. Effect of ATP synthesis promotors on postischemic myocardial recovery. J Surg Res 1990; 49:205–11.
16. Ledingham S, Katayama O, Lachno D, Patel N, Yacoub M. Beneficial effect of adenosine during reperfusion following prolonged cardioplegic arrest. Cardiovasc Res 1990;24: 247–53.
17. Petsikas D, Ricci MA, Baffour R, de Varennes B, Symes J, Guerraty A. Enhanced 24-hour in vitro heart preservation with adenosine and adenosine monophosphate. J Heart Transplant 1990;9:114–8.
18. Demmy TL, Magovern JA, Kao RL, Magovern GJ. Resuscitation of injured myocardium with adenosine and biventricular assist. Ann Thorac Surg 1991;52:1044–51.
19. Robinson LA, Braimbridge MV, Hearse DJ. Enhanced myocardial protection with high-energy phosphates in St. Thomas' Hospital cardioplegic solution. J Thorac Cardiovasc Surg 1987;93:415–27.

Effect of Prostaglandin I_2 and Superoxide Dismutase on Reperfusion Injury of Warm Ischemic Lung

Chojiro Yamashita, MD, Hidefumi Oobo, MD, Fukumasa Tsuji, MD, Satosi Tobe, MD, Hidehiro Yamamoto, MD, Hiroomi Nakamura, MD, Masayosi Okada, MD, and Kazuo Nakamura, MD

Second Division, Department of Surgery, Kobe University School of Medicine, Kobe, Japan

A prostaglandin I_2 (PGI_2) analogue and superoxide dismutase (SOD) were administered to dogs with pulmonary denervation, and their effects on warm ischemic damage to the lung were studied. Twenty-seven adult mongrel dogs were divided into a control group (6 dogs), a PGI_2 group (7 dogs), an SOD group (6 dogs), and a heparin group (8 dogs). The left pulmonary hilum was dissected, with PGI_2 (1 μg/kg) being administered to the PGI_2 group and heparin (100 U/kg) to the heparin group. Then the left lung was placed in a warm ischemic state for 1 hour. The SOD group also received 20 mg/kg of SOD intravenously 1 minute before reperfusion. Before warm ischemia, immediately after reperfusion, and 1 hour and 2 hours afterward, the blood gases, left pulmonary vascular resistance, and other data were measured under right pulmonary artery clamping. Arterial oxygen tension showed significantly better values in the SOD and PGI_2 groups than in the control and heparin groups. The left pulmonary vascular resistance increased with time in the control group but did not increase in the PGI_2 group. Pulmonary microangiography showed that dilatation of the pulmonary arterioles was prominent in the PGI_2 group. The quantity of pulmonary extravascular fluid was significantly less in the PGI_2 and SOD groups than in the control and heparin groups. Histological examination showed marked collapse of capillaries, intraalveolar hemorrhage, and edema in the control and heparin groups, whereas these changes were only slight in the PGI_2 and SOD groups. Thus, both PGI_2 and SOD appeared to have a protective effect on the pulmonary microcirculation and tissue, and may be effective in preventing warm ischemic damage in lung transplantation.

(Ann Thorac Surg 1992;54:921–4)

In lung transplantation, the appearance of infiltrates in the transplanted lung is seen on postoperative chest roentgenograms along with a decrease in respiratory function and worsening of the blood gases, and this transient pulmonary impairment is called the reimplantation response. It would be desirable to distinguish these events from rejection, elucidate the underlying mechanism, and develop methods to prevent the occurrence of these early postoperative phenomena. Warm ischemic damage, denervation, and the interruption of lymphatics have all been considered as possible causes of the reimplantation response. Prostaglandin I_2 (PGI_2) inhibits platelet aggregation, causes vasodilatation, is cytoprotective, and stabilizes lysosome membranes, so we considered that it might be possible to reduce the reimplantation response by using a PGI_2 analogue. In unilateral pulmonary transplantation, unlike cardiac transplantation, blood at a temperature of about 36°C enters the transplanted lung at the time of reperfusion, and damage from oxygen radicals is likely to occur. Therefore, the radical scavenger superoxide dismutase (SOD) might also be effective against warm ischemic reperfusion disturbance, and we studied its role in a pulmonary denervation model.

Material and Methods

Twenty-seven adult mongrel dogs weighing 10 to 15 kg were divided into four groups: 6 dogs formed the control group, 7 dogs were in the PGI_2 group, 6 dogs formed the SOD group, and 8 dogs were in the heparin group. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institute of Health (NIH publication No. 85-23, revised 1985). General anesthesia was induced with ketamine hydrochloride (Ketalar; Parke-Davis, Morris Plains, NJ; 10 mg/kg), thiamylal sodium (Yoshitomi Inc, Osaka, Japan; 20 mg/kg), and pancuronium bromide (Mioblock; Organon Inc, West Orange, NJ; 1 mg/kg), and a volume-controlled ventilator was used to provide ventilation (inspired oxygen fraction, 0.60; internal airway pressure, 15 cm H_2O; ventilation rate, 20/min). Next, an arterial line was inserted into the right carotid artery and a Swan-Ganz catheter was advanced to the pulmonary artery trunk through the jugular vein. Arterial and mixed venous blood gases were measured, and then thoracotomy was performed through the fourth left inter-

---

Accepted for publication March 6, 1992.

Address reprint requests to Dr Yamashita, Second Division, Department of Surgery, Kobe University School of Medicine, 7-5-2 Kusunoki-cho Chuoku, Kobe, Japan 650.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

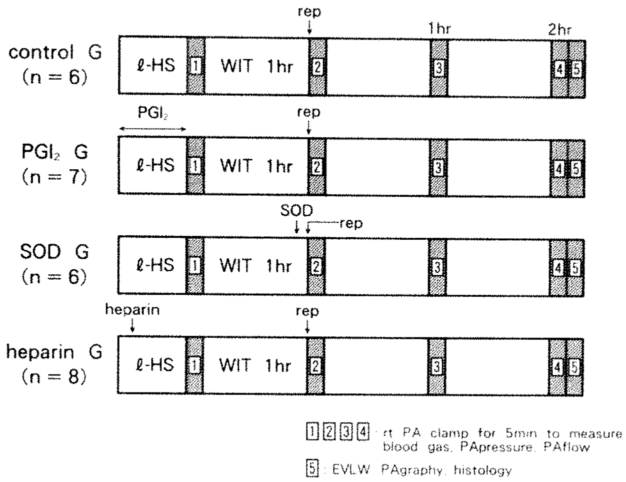


Fig 1. Protocol of the experiment. Arrows *indicate the time of administration of prostaglandin I_2 (PGI_2), superoxide dismutase (SOD), and heparin.* Shaded squares *show the time of measurement. (EVLW = extravascular lung water;* l-HS = *left hilar stripping;* PA = *pulmonary artery;* PAgraphy = *pulmonary arteriography;* rep = *reperfusion;* WIT = *warm ischemic time.)*

costal space. The left pulmonary artery, pulmonary vein, and main bronchus were dissected out, and after the nerves, bronchial arteries, and lymphatics were completely transected, the right and left pulmonary arteries were taped. During this procedure, a PGI_2 analogue (1 μg/kg) was administered through the Swan-Ganz catheter in the pulmonary artery over a 30-minute period in the PGI_2 group.

In the heparin group, heparin (100 U/kg) was injected intravenously during dissection of the hilum. Next, an electromagnetic flow meter was attached to the pulmonary artery trunk, and the right pulmonary artery was clamped to evaluate hemodynamics in the left lung. Ventilation was performed at an inspired oxygen fraction of 1.0 for 5 minutes and then the blood gases, pulmonary artery pressure, and pulmonary arterial blood flow were measured to provide standard values. Thereafter, the right pulmonary artery was released and the left lung was deflated. Then the left pulmonary artery and vein and the main bronchus were clamped with a vascular clamp for 1 hour to produce warm ischemia of the left lung. In the SOD group, 20 mg/kg of SOD was injected intravenously 1 minute before reperfusion. Immediately after reperfusion as well as 1 hour and 2 hours afterward, measurements were performed to investigate lung function, and then the heart and lungs were excised. Extravascular fluid in the left lung was determined by the dry weight method in 5 animals from each group. In the remaining dogs of each group (1 in the control group, 2 in the PGI_2 group, 1 in the SOD group, and 3 in the heparin group), 50% barium solution was injected from the pulmonary artery trunk into both lungs at a pressure of 30 cm H_2O to perform soft roentgenography. The plates were enlarged 10 times for comparative study (microangiography). Finally, a histological study was performed (Fig 1).

The results were expressed as a mean value and standard error. Statistical significance was determined by two-factorial analysis of variance and the *t* test. A *p* value less than 0.05 was considered to be significant.

Results

The following data were measured under clamping of the right pulmonary artery to evaluate left lung function after warm ischemia. Arterial oxygen tension decreased with time in both the control and heparin groups, but remained stable at 280 to 360 mm Hg in both the PGI_2 and SOD groups. Significant differences were noted between the PGI_2 and SOD groups and the control and heparin groups at 1 hour and 2 hours after reperfusion (Fig 2). Arterial carbon dioxide tension showed a slow increase with time in all four groups, but no significant difference was seen among them.

The left pulmonary vascular resistance was high in all groups, and it was noted that the cardiac output was only about 1 L/min in small dogs weighing 10 to 15 kg. Before warm ischemia, left pulmonary vascular resistance was 1,800 to 2,200 dyne · s · cm^{-5} in all four groups, but it increased sharply in the control and SOD groups after 2 hours of reperfusion to become 5,780 ± 681 and 5,005 ± 1,459 dyne · s · cm^{-5}, respectively. However, in the PGI_2 group it increased only slightly to 2,137 ± 205 dyne · s · cm^{-5} immediately after reperfusion and to 2,748 ± 347 dyne · s · cm^{-5} after 2 hours. In the heparin group, left pulmonary vascular resistance increased moderately to 2,775 ± 261 dyne · s · cm^{-5} immediately after reperfusion and to 3,695 ± 278 dyne · s · cm^{-5} after 2 hours. But significant differences were noted between PGI_2 group and control group only at 2 hours after reperfusion (Fig 3).

The left extravascular lung water content was 6.99 mL/kg in the control group and 6.02 mL/kg in the heparin group. It was significantly lower in the PGI_2 and SOD groups, being 4.93 mL/kg and 4.36 mL/kg, respectively (Fig 4).

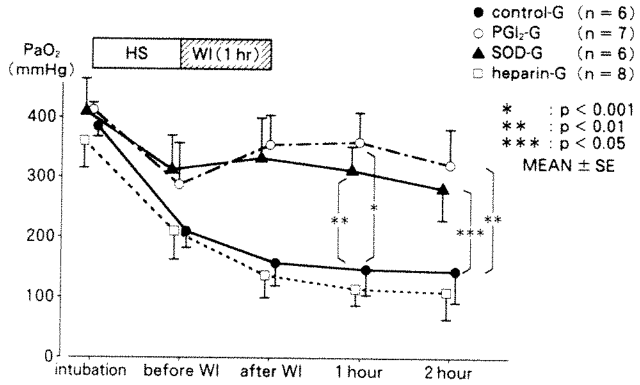


Fig 2. Arterial oxygen tension (PaO_2) during occlusion of the right pulmonary artery before warm ischemia of the left lung, just after reperfusion, and 1 and 2 hours afterward. Significant differences were noted between the prostaglandin I_2 (PGI_2) and superoxide dismutase (SOD) groups and the control group at 1 and 2 hours after reperfusion. (HS = hilar stripping; WI = warm ischemia.)

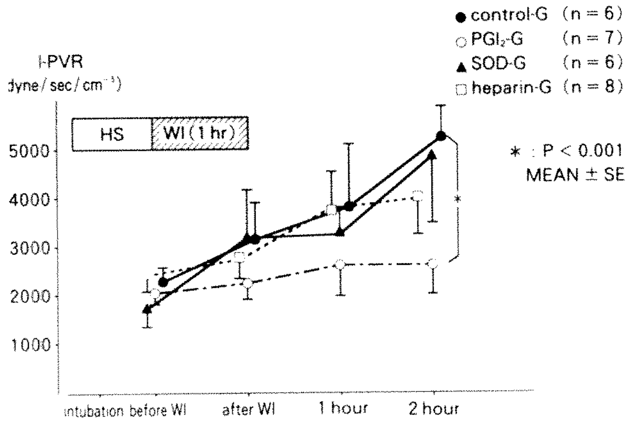


Fig 3. Left pulmonary vascular resistance (l-PVR) during occlusion of the right pulmonary artery before warm ischemia of the left lung, just after reperfusion, and 1 and 2 hours afterward. A significant difference was seen between the prostaglandin I_2 (PGI$_2$) group and control group at 2 hours after reperfusion. (HS = hilar stripping; SOD = superoxide dismutase; WI = warm ischemia.)

In postmortem pulmonary microangiography, the contrast medium did not reach the periphery of the left pulmonary arterial vasculature in both the control and heparin groups, and occlusion of vessels of 100 to 200 μm in diameter was seen. The SOD group showed similar findings. In the PGI$_2$ group, however, the vascular tree was visualized clearly to a level of less than 100 μm in diameter, and little difference was noted when compared with the right lung, which had not been manipulated (Fig 5).

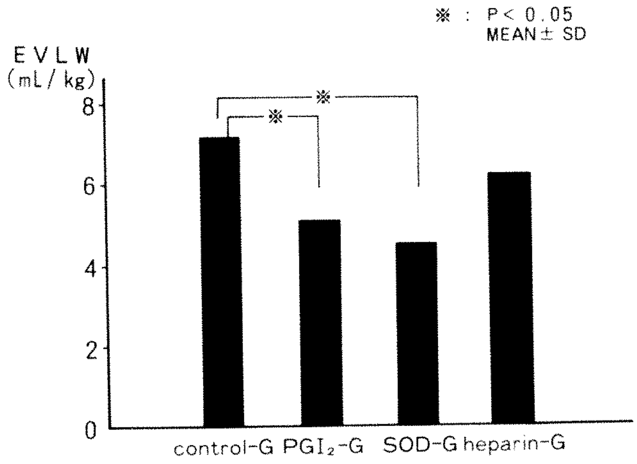


Fig 4. The left extravascular lung water (EVLW) content: EVLW was significantly lower in the prostaglandin I_2 (PGI$_2$) and superoxide dismutase (SOD) groups than in the control group.

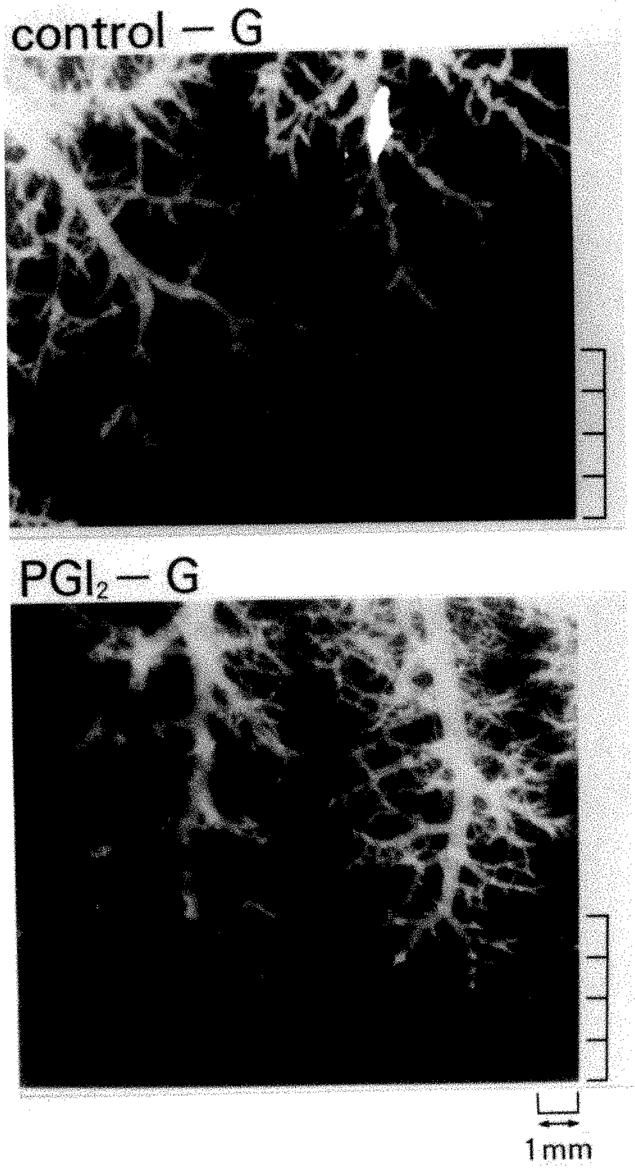


Fig 5. By postmortem pulmonary microangiography, the pulmonary vascular tree was visualized clearly to the level of less than 100 μm in the prostaglandin I_2 (PGI$_2$) group, but contrast medium did not reach these small arterioles in the superoxide dismutase, control, and heparin groups.

In the control and heparin groups, alveolar hemorrhage, exudate, and interstitial edema were prominent on histologic examination. The capillaries were narrow and collapsed. Sludging in the capillaries was seen in the control group. In the SOD group, alveolar edema and hemorrhage were very slight and the alveolar architecture was almost normal. In the PGI$_2$ group, alveolar hemorrhage and exudates were noted occasionally. Dilatation of the pulmonary arterioles was prominent, and a marked increase of blood flow was noted as far distally as the capillaries.

Comment

Cause of the Reimplantation Response

The reimplantation response is a transient state of pulmonary edema occurring after transplantation, and warm ischemic reperfusion injury, chemical mediators, denervation, or operative manipulation are all regarded as possible causes [1–3]. Warm ischemic reperfusion injury includes cellular disturbances due to ischemia itself and other disturbances occurring at the time of reperfusion [4]. Because the lung contains air, unlike other organs, cellular function is maintained even after warm ischemia lasting for 2 to 3 hours [5–7], but interstitial edema, hemorrhage, and the destruction and swelling of mitochondria have been shown to develop after 60 minutes of warm ischemia [8]. Furthermore, because pulmonary edema becomes more marked with the increase in warm ischemic time, there is no doubt that warm ischemia is an important cause of the reimplantation response. When an organ undergoes warm ischemia, lipid peroxidation and the no-reflow phenomenon can occur. Free radicals are produced in the endothelial cell membranes and in neutrophils at the time of reperfusion and cause an increase in cell membrane permeability [9, 10]. Superoxide dismutase is reported to scavenge free radicals produced by the hypoxanthine-xanthine oxidase system and by neutrophils, and to inhibit reperfusion injury by suppressing membrane lipid peroxidation [11–13]. The no-reflow phenomenon occurs when, after warm ischemia and reperfusion, the blood does not flow sufficiently from the arterioles to the capillaries due to sludging of red blood cells, obstruction by white blood cells, vasospasm, and narrowing of the vessel lumen due to edema of the vascular endothelium [14]. These reperfusion disturbances are also regarded as important causes of the reimplantation response.

In this study, we investigated the effect of PGI_2 and SOD on reperfusion injury of the warm ischemic lung. We used a hilar-stripped lung model with additional warm ischemia instead of an autotransplantation model to make warm ischemic time equal. However, we believe that the purpose of this study concerning reperfusion injury was achieved by comparison with the control group.

Effects of Prostaglandin I_2 and Superoxide Dismutase

In the control group, deterioration of blood gases, an increase in pulmonary vascular resistance, an increase in the pulmonary extravascular water content, microcirculatory damage, and red cell sludging were noted immediately after operation. Arterial oxygen tension in the PGI_2 and SOD groups was well maintained even after reperfusion, and there was a significant difference between the control group and the PGI_2 and SOD groups at 1 and 2 hours after reperfusion. Pulmonary vascular resistance in the PGI_2 group did not increase after reperfusion, and a significant difference was noted between the PGI_2 group and the control group at 2 hours after reperfusion. From these phenomena, the microcirculation was probably improved by such actions of PGI_2 as the inhibition of platelet aggregation, relaxation of vascular smooth muscle, inhibition of white cell adhesion, and its cytoprotective effect [15–18]. Furthermore, it was considered that tissue damage was probably reduced along with the improvement of blood gases through the prevention of an increase in capillary hydrostatic pressure by obviating a rise in pulmonary artery pressure. Also, the inhibition of chemical mediators such as thromboxanes and the cytoprotective action of PGI_2 would have had some effect. Although red cell sludging in the capillaries was prevented by the administration of heparin, an increase in pulmonary vascular resistance and the deterioration of blood gases were still noted. Accordingly, the heparin could not maintain pulmonary function after warm ischemia and hilar stripping of the lung. With the administration of SOD, as with PGI_2 pulmonary function was well maintained after warm ischemia, and the histological study showed that pulmonary edema was inhibited and the alveolar architecture remained nearly normal. These findings indicated that reperfusion injury was reduced by the administration of PGI_2 or SOD. However, because an increase in pulmonary vascular resistance was noted in the SOD group and also because microangiography did not visualize the smaller pulmonary arterioles, the action of SOD on the pulmonary circulation was considered to be less effective than that of PGI_2.

References

1. Veith FJ, Koerner SK. The present status of lung transplantation. Arch Surg 1974;109:734–40.
2. Veith FJ, Kamholz SL, Mollenkoph FP, Montefusco CM. Lung transplantation 1983. Transplantation 1983;35:271–7.
3. Prop J, Ehrie MG, Crapo JD, Nieuwenhuis P, Wildevuur CRH. Reimplantation response in isografted rat lung. Analysis of causal factors. J Thorac Cardiovasc Surg 1984;87: 702–11.
4. Handa M, Fujimura S, Kondo O, Nakata Y. Lung preservation. Jpn Ann Thorac Surg 1987;40:174–9.
5. Hitomi S, Wada H, Aoki M, et al. Lung transplantation. Jpn J Thorac Surg 1987;40:180–5.
6. Itinose T, Handa M, Hujimura S, et al. Warm ischemic time in lung transplantation. J Jpn Assoc Chest Surg 1987;1:101.
7. Toledo-Pereyra LH, Hau T, Simmons RL, Najarian JS. Lung preservation techniques. Ann Thorac Surg 1977;23:487–94.
8. Nishida T, Shibata H, Koseki M. Peroxidative injury of the mitochondrial respiratory chain during reperfusion of hypothermic rat liver. Biochem Biophys Acta 1987;890:82–8.
9. Mead JF. Free radical mechanisms of lipid damage and consequences for cellular membranes. Free Radic Biol 1976; 1:51–68.
10. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 1985;312:159–63.
11. Parks DA, Granger DN. Xanthine oxidase: biochemistry, distribution and physiology. Acta Physiol Scand 1986;548: 87–99.
12. Makino R, Tanaka T, Iizuka T, Ishimura Y, Kanegasaki S. Stoichiometric conversion of oxygen to superoxide anion during the respiratory burst in neutrophils. J Biol Chem 1986;261:11444–7.
13. Bannister JV, Bannister WH, Rotilio G. Aspects of structure, function and applications of superoxide dismutase. CRC Crit Rev Biochem 1987;22:111–80.
14. Braunwald E, Kloner RA. Myocardial reperfusion: a double-edged sword. J Clin Invest 1985;76:1713–9.
15. Hirose T. Pulmonary edema. Gendaiiryo 1986;18:2642–51.
16. Hirose T. Respiratory organ and prostaglandin. Rinsyoukagaku 1981;17:1047–54.
17. Czer GT, Marsh J, Konopka R, Moser KM. Low-dose PGI_2 prevents monocrotaline-induced thromboxane production and lung injury. J Appl Physiol 1986;60:464–71.
18. Kambayashi J, Hatayama K, Kajiwara M, Sakon M, Oshiro T, Mori T. Mechanism of the cytoprotective effect of prostaglandin I_2 and its analogue in human platelets. Thromb Res 1986;44:439–44.

Comparison of 180-Degree and 360-Degree Skeletal Muscle Nerve Cuff Electrodes

George V. Letsou, MD, James F. Hogan, BSEE, Philip Lee, MS, Jung H. Kim, MD,
Stephan Ariyan, MD, Michael L. Dewar, MD, John C. Baldwin, MD, and
John A. Elefteriades, MD

Departments of Surgery and Pathology, Yale University, New Haven, Connecticut, and Medtronic, Inc, Minneapolis, Minnesota

Use of skeletal muscle for cardiac augmentation is a promising technique for treatment of end-stage cardiac failure. An electrode woven through the latissimus dorsi that recruits nearby nerve fibers is commonly used to pace skeletal muscles both in clinical practice and in the laboratory. A proximally placed nerve cuff electrode offers potential advantages in improved recruitment of muscle fibers and low threshold for stimulation. We tested the effectiveness of a nerve cuff electrode passed directly about the proximal thoracodorsal nerve. Our report looks at the efficacy of nerve cuff electrode stimulation and compares electrical and histologic characteristics of a 180-degree wrap of the thoracodorsal nerve to a 360-degree wrap in dogs over 3 months. Threshold voltage at the commonly used pulse width of 200 microseconds was typically in the range of 400 to 600 mV for each electrode after 3 months. Statistical analysis revealed no significant difference ($p < 0.05$) in threshold voltage or current between the 180-degree and 360-degree nerve cuff electrode either at acute evaluation or after 3 months. Even contraction of latissimus dorsi was achieved with all implants. Adenosine triphosphatase staining revealed 100% conversion of type II to type I fibers in all stimulated muscles. Histologic examination of the thoracodorsal nerve and latissimus dorsi muscle revealed no abnormalities grossly or by light microscopy. Thus, a carefully applied nerve cuff electrode is an atraumatic, effective method for skeletal muscle stimulation. The 180-degree and 360-degree nerve cuff configurations are equally effective.

(Ann Thorac Surg 1992;54:925–31)

Use of skeletal muscle for cardiac augmentation and hemodynamic support is a promising technique for end-stage cardiac disease not amenable to conventional treatment modalities. Experimental work has been ongoing and productive for more than a decade [1, 2]. Recent reports document its clinical applicability [3, 4].

To date, latissimus dorsi muscle has been used most frequently. Stimulation has been achieved through a number of methods, but most clinical efforts have used a pair of intramuscular electrodes weaved through muscular tissue. These electrodes recruit nearby nerve fibers in muscular tissue. We have developed an alternative electrode that is atraumatic and stimulates the proximal thoracodorsal nerve trunk directly [5]. This electrode is very similar to electrodes used for clinical peripheral nerve stimulation, to those used in experimental skeletal muscle ventricles, and to those used in our large clinical experience with phrenic nerve stimulation [1, 6]. A flat platinum alloy surrounded by silicone rubber on one side (Medtronic, Inc, Minneapolis, MN) is applied directly to the isolated proximal thoracodorsal nerve in either a 180-degree or 360-degree configuration (Fig 1). Muscular stimulation is achieved by sending a train of pulses through the electrode via a wire covered with silicone rubber.

Our objective was to test the effectiveness of both the 180-degree and 360-degree electrode conformations in achieving muscular stimulation. Threshold voltage and current were measured both in the acute setting (just after electrode placement) and after 3 months of chronic stimulation. Threshold power and energy were calculated from these values. Biopsy of thoracodorsal nerve and latissimus dorsi muscle was performed at 3 months to assess functional status (after measurement of threshold voltage and current).

Material and Methods

Surgical Procedures

Thirteen mongrel dogs weighing 25 to 35 kg were used. At the initial operation, all animals were fully anesthetized using pentobarbital (20 mg/kg) intravenously and halothane (0.5% to 1.5%) as an inhalational anesthetic. A volume ventilator (Harvard Apparatus Co, Inc, Millis, MA) was used to administer inhalational anesthetic and oxygen. After induction of anesthesia, animals were placed in the supine position. Bilateral incisions were made ventral to both latissimus dorsi muscles. Each latissimus was dissected away from the body wall leaving proximal and distal insertions intact. Each thoracodorsal nerve was isolated high in the axilla. In 6 animals a 180-degree nerve cuff electrode (Medtronic, Inc) was

---

Accepted for publication March 11, 1992.

Address reprint requests to Dr Letsou, Section of Cardiothoracic Surgery, Yale University School of Medicine, 121 FMB, 333 Cedar St, New Haven, CT 06510.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

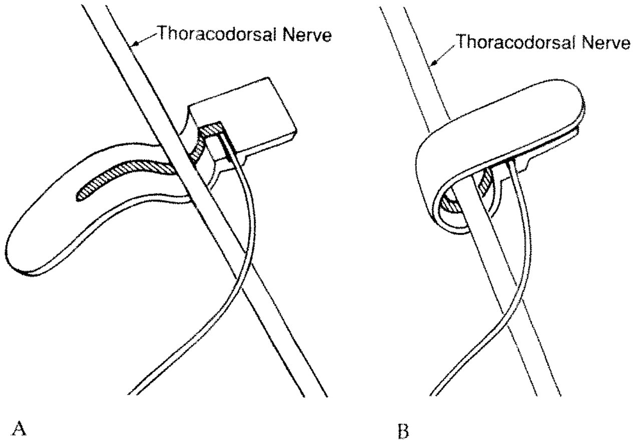


Fig 1. The two electrode configurations for stimulation of thoracodorsal nerve: (A) 180-degree or "half cuff" configuration, (B) 360-degree or "full cuff" configuration.

Table 1. Pacing Schedule Followed in All Animals After Electrode Implantation[a]

Week After Recovery From Operation	Frequency (Hz)	Pulse Width (μs)	On Time (s)	Off Time (s)	Muscle Contractions Per Minute
1	10	150	0.25	2.0	26
2	10	150	0.25	1.5	34
3	10	150	0.25	1.0	48
4	10	150	0.25	0.75	60
5–12	25	150	0.13	0.69	73

[a] Voltage amplitude maintained at 2 to 3 times visual threshold.

applied bilaterally (see Fig 1A). Application involved a very limited, gentle dissection of the thoracodorsal nerve away from surrounding tissues and application of the nerve cuff by sliding it under the thoracodorsal nerve. The silicone rubber cuff was fixed to surrounding tissue using two 4-0 polypropylene interrupted sutures. In 7 other animals, a 360-degree nerve cuff electrode (Medtronic, Inc) was applied bilaterally in a similar fashion (see Fig 1B). The 360-degree nerve cuffs were applied meticulously. Cuff diameter was adjusted to 2 to 3 times the diameter of the thoracodorsal nerve. Threshold strength-duration curves were performed on each electrode as described below.

On one side of each animal the electrode lead was attached to an Itrel 7421 pulse train stimulator (Medtronic, Inc). On the other side, the lead was capped and buried in subcutaneous tissue. Wounds were closed in standard fashion. All animals then recovered from this first operation. Figure 2 diagrams the experimental protocol.

After all surgical wounds had healed (7 to 14 days), the pulse train stimulator was activated and muscle conditioning begun on one side of each animal. Pacing parameters were adjusted progressively as outlined in Table 1. Stimulation frequency was 10 Hz for the first 4 weeks of conditioning and 25 Hz for the final 8 weeks. Pulse width was maintained at 150 microseconds throughout. The on-time and off-time of the pulse train was altered such that the number of muscle contractions per minute increased from 26 during the first week of stimulation to 73 per minute for the final 8 weeks. The voltage amplitude was maintained at 2 to 3 times the visual threshold, which was determined every 2 weeks. "Visual threshold" was the minimal voltage required for muscular stimulation.

After 3 months of conditioning, all animals were anesthetized using pentobarbital and halothane as described

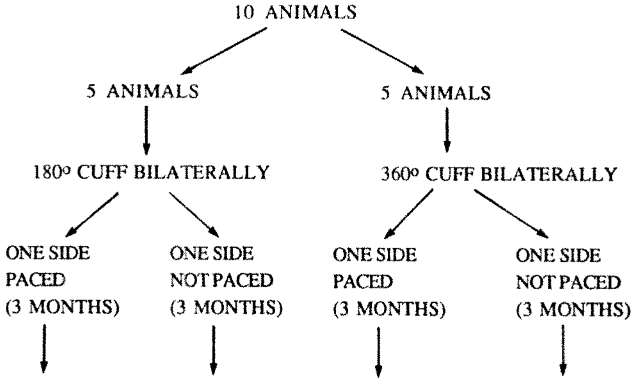

10 ANIMALS
5 ANIMALS
5 ANIMALS
180° CUFF BILATERALLY
360° CUFF BILATERALLY
ONE SIDE PACED (3 MONTHS)
ONE SIDE NOT PACED (3 MONTHS)
ONE SIDE PACED (3 MONTHS)
ONE SIDE NOT PACED (3 MONTHS)
SACRIFICE
SACRIFICE
SACRIFICE
SACRIFICE

Fig 2. Scheme of experimental protocol. Six animals had 180-degree cuff electrodes placed but 1 was discarded from the analysis because of an infection on the unstimulated side. Seven animals had 360-degree cuff electrodes placed but 2 were discarded from the analysis (see text).

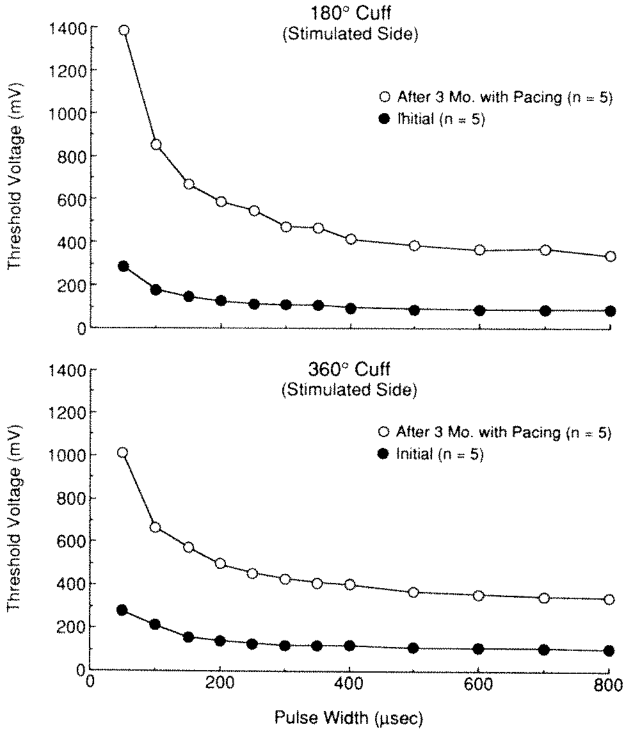


Fig 3. Comparison of average threshold voltage strength-duration curves for the 180-degree and 360-degree electrodes at time of implantation and after 3 months of stimulation. Each point represents the average threshold voltage for 5 animals at a given pulse width. See text for further explanation.

previously. Each animal had both latissimus dorsi muscles dissected away from the chest wall. As in the initial operation, both proximal origins and distal insertions were left intact. The free end of each nerve cuff electrode was isolated and connected to a pulse train stimulator. Strength-duration curves for each electrode were again determined as described below. After these curves had been generated bilaterally, a fresh biopsy specimen of each latissimus muscle belly was obtained. For muscle histochemistry, a small fragment of muscle was immediately frozen in isopentane prechilled in liquid nitrogen. Ten-micrometer-thick frozen sections were made from the frozen muscle, and they were stained with hematoxylin and eosin, modified Gomori trichrome, periodic acid-Schiff, nicotinamine adenine dinucleotide (reduced form) (NADH), and adenosine triphosphatase (pH 9.6) as described by Dubowitz and Brooke [7]. For histological examination of the nerve, nerve segments were obtained 1 cm proximal and distal to the electrode cuff and at the electrode cuff as well. After fixation with 10% buffered formalin, nerve segments were routinely processed for dehydration and paraffin embedding. Six-micrometer-thick sections were stained with hematoxylin and eosin, Luxol fast blue for the myelin sheath, and Sevier-Munger silver technique for axons. The animal was then sacrificed.

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" and the

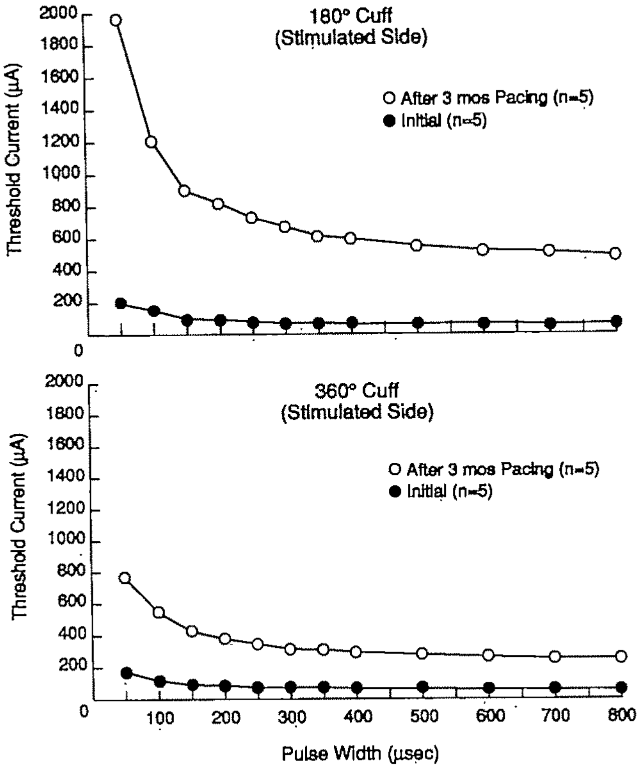


Fig 4. Comparison of average threshold current strength-duration curves for the 180-degree and 360-degree electrodes at time of implantation and after 3 months of stimulation. Each point represents the average threshold current for 5 animals at a given pulse width. See text for further explanation.

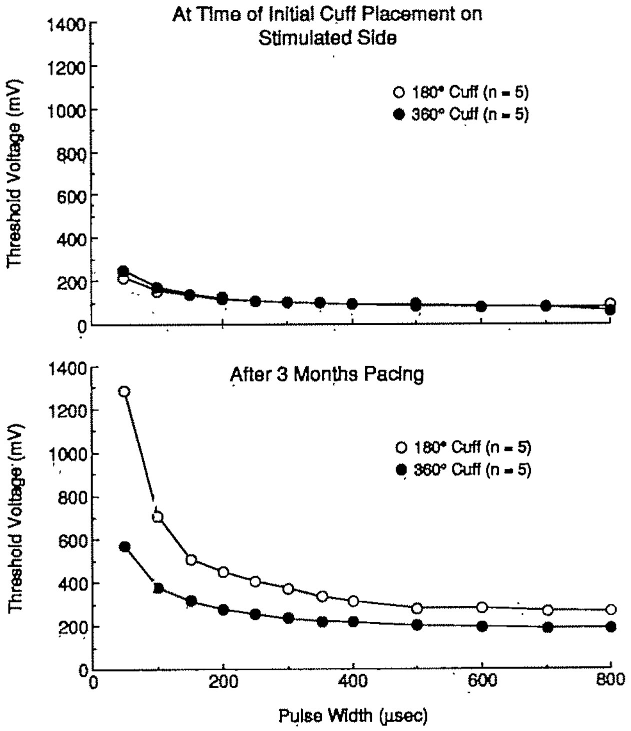


Fig 5. Comparison of average threshold voltage strength-duration curves for the 180-degree and 360-degree electrodes at the time of implantation (top) and after 3 months of pacing (bottom). Each point represents the average threshold voltage for 5 animals at a given pulse width. See text for further explanation.

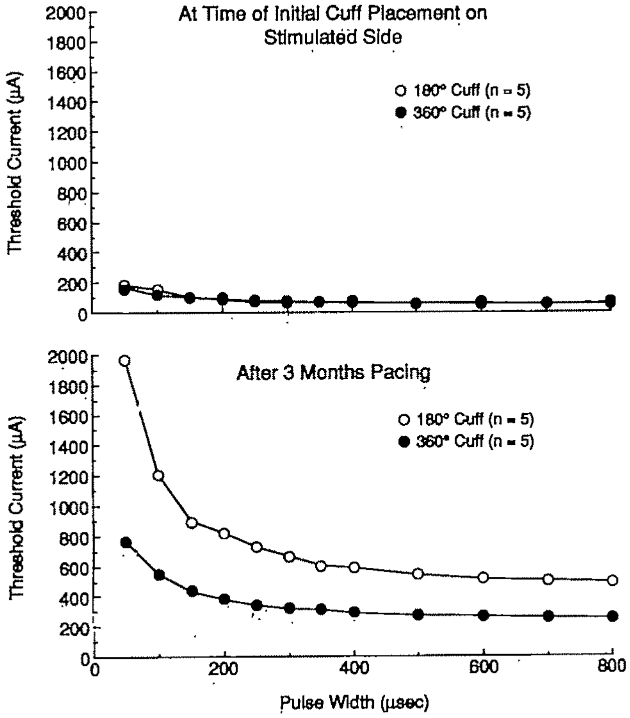


Fig 6. Comparison of average threshold current strength-duration curves for the 180-degree and 360-degree electrodes at the time of implantation (top) and after 3 months of pacing (bottom). Each point represents the average threshold current for 5 animals at a given pulse width. See text for further explanation.

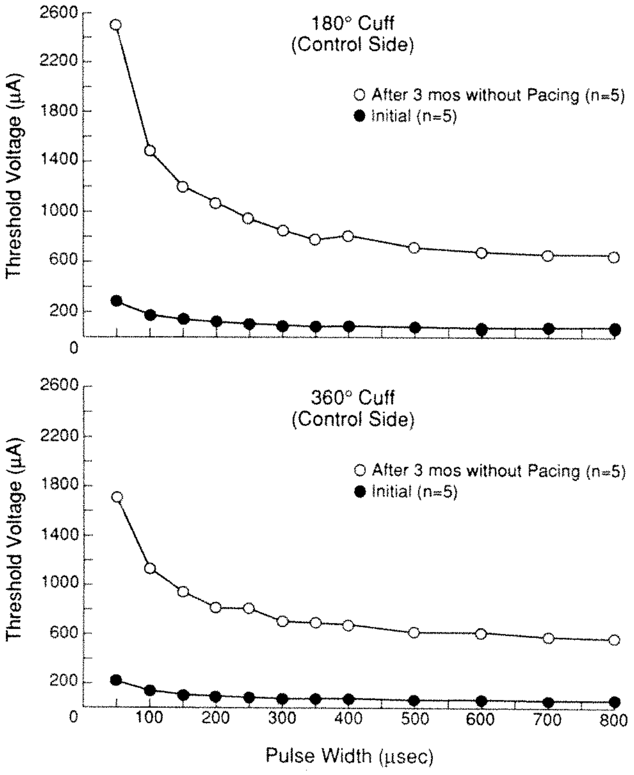


Fig 7. Comparison of average threshold voltage strength-duration curves for the 180-degree and 360-degree electrodes at the time of implantation and 3 months later on the side of each animal that was not stimulated (control side). Each point represents the average threshold voltage for 5 animals at a given pulse width. See text for further explanation.

"Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institute of Health (NIH publication No. 85-23 revised 1985). The Yale University Animal Care and Use Committee approved and regulated all animal care.

Determination of Strength-Duration Curves

Threshold determinations were made using a stimulator designed in our laboratory that allowed voltage amplitude and pulse duration of the applied stimulus to be varied. The output was of constant voltage and continuously variable from 0 to 10 V with a pulse width adjustable from 50 to 800 microseconds. The cathodal output was applied to the nerve electrode and the anodal output to an indifferent electrode (Avery Laboratories, Glenn Cove, NY) buried in subcutaneous tissue at each analysis. For visual threshold determinations, the pulses were applied at a rate of 30 pulses per minute. After presetting pulse duration, stimulus amplitude was slowly increased until muscle twitches were just discernible. Using a battery-powered oscilloscope (model 211; Tektronix, Beaverton, OR) to prevent ground loops, the pulse voltage was measured. The pulse current was calculated by measuring the voltage drop across a precision 100-Ω resistor connected in series with the electrode. Threshold determinations were made at 50-microsecond intervals from 50 to 400 microseconds and then at 100-microsecond intervals from 400 to 800 microseconds. Strength-duration curves for voltage and current were generated from these determinations.

Statistics

Analysis was performed on 10 animals. Three animals were discarded from the analysis because of technical problems. One animal with a 180-degree nerve cuff placed bilaterally developed an infection on the unstimulated side. Two animals with 360-degree nerve cuff electrodes had complications on the unstimulated control side (one infection and one possible nerve degeneration). This left 5 animals with 180-degree nerve cuffs placed bilaterally and 5 animals with 360-degree nerve cuffs placed bilaterally. A comparison of strength-duration curves was carried out using the two-factor repeated measures analysis of variance. Analysis of covariance was used to verify the relationship between the two parameters. A p value of less than 0.05 was considered significant.

Results

Electrical Studies (strength-duration curves)

All 10 animals that successfully completed the entire experimental protocol (5 with 180-degree nerve cuff electrodes and 5 with 360-degree nerve cuff electrodes) had strength-duration curves determined both at the time of

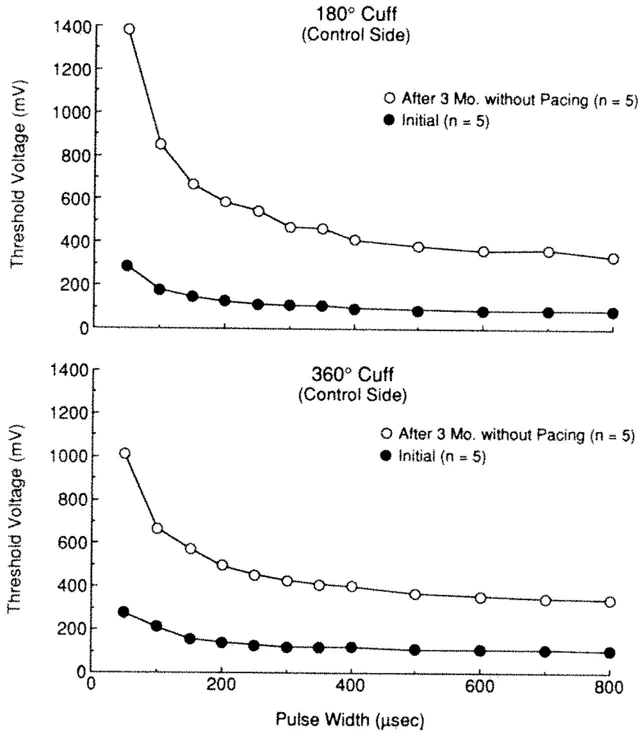


Fig 8. Comparison of average threshold current strength-duration curves for the 180-degree and 360-degree electrodes at the time of implantation and 3 months later on the side of each animal that was not stimulated (control side). Each point represents the average threshold current for 5 animals at a given pulse width. See text for further explanation.

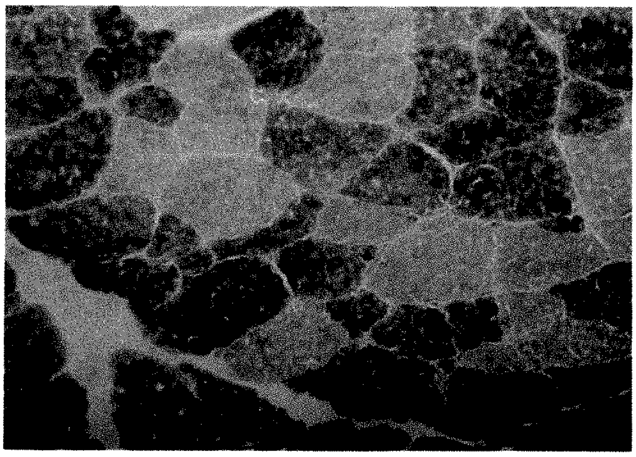


Fig 9. Adenosine triphosphatase stain of unconditioned normal canine latissimus dorsi. There are approximately 50% darker staining type II fast-twitch fibers and 50% lighter staining type I slow-twitch fibers.

initial electrode placement and 3 months later at sacrifice. Strength-duration curves were determined by observing threshold voltage and current across a range of pulse widths from 50 microseconds to 800 microseconds. Figure 3 graphically compares the threshold voltages of the 180-degree nerve cuff electrode and the 360-degree nerve cuff electrode on the animals' stimulated side at the time of initial placement and after 3 months of pacing. After 3 months of pacing, both the 180-degree nerve cuff electrode and the 360-degree nerve cuff electrode demonstrated a statistically significant ($p < 0.05$) increase in threshold voltage. Also of note was the low threshold voltage (in the range of 0.4 to 0.5 V at 150-millisecond pulse width) for both electrode configurations even at 3 months. The findings for threshold current were similar with a statistically significant ($p < 0.05$) increase after 3 months of pacing (Fig 4).

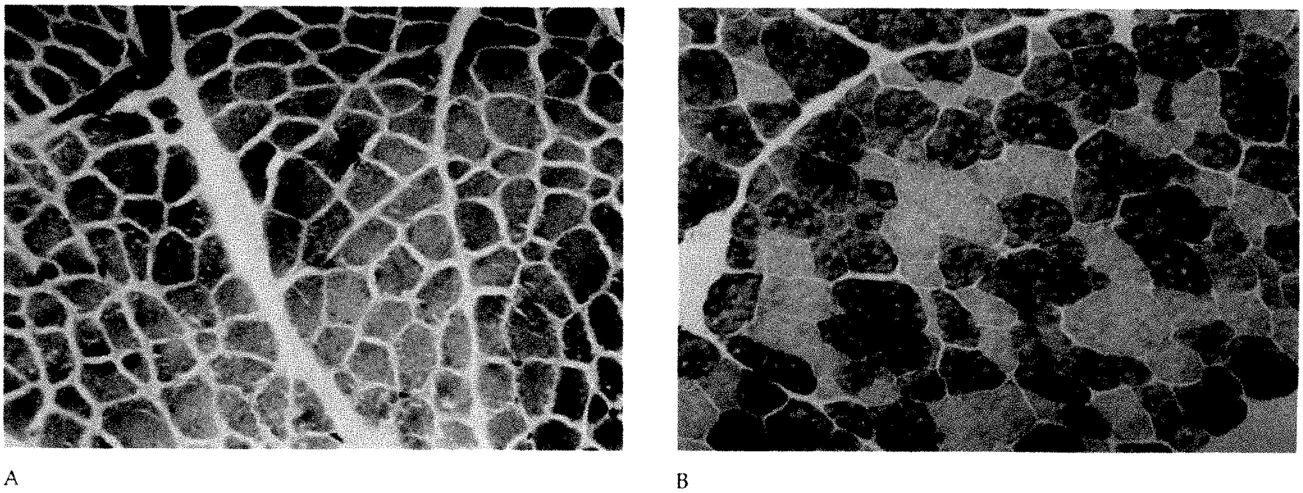
Figures 5 and 6 graphically illustrate a comparison of threshold voltage and current for the two electrode configurations at the time of initial placement and after 3 months of pacing. A comparison of threshold voltage for the two electrodes at the time of initial placement is shown in Figure 5 (top). There is no statistically significant difference in threshold voltage at the $p < 0.05$ level. A similar comparison of threshold current, shown in Figure 6 (top), also reveals no statistically significant difference between the two electrodes. After 3 months of pacing, there is no statistically significant difference in threshold voltage or current for the two electrode configurations (as illustrated in Figures 5 [bottom] and 6 [bottom]), although there is a trend for the 360-degree nerve cuff electrode to have lower threshold voltage and current.

Threshold voltage and current also increased on the unstimulated (control) side of each animal. Figure 7 (top) shows this increase in threshold voltage for the 180-degree nerve cuff electrode on the control side of the 5 animals with this nerve cuff configuration. The two curves are significantly different ($p < 0.05$). A separate analysis (Fig 8 [top]) also showed a statistically significant ($p < 0.05$) increase in threshold current in the 180-degree electrode after 3 months. The 360-degree nerve cuff electrode on the control side on each animal (see Fig 7 [bottom] and Fig 8 [bottom]) showed a similar statistically significant increase in threshold voltage and current after 3 months without pacing.

When strength-duration curves for threshold voltage and current obtained from 360-degree nerve cuff electrodes on the control side of each animal after 3 months were compared with those obtained from 360-degree nerve cuff electrodes on the stimulated side of each animal after 3 months, there was no statistically significant difference in the curves. The 180-degree nerve cuff electrodes behaved similarly. Thus, an increase in threshold voltage and current was seen whether or not stimulation was carried out.

Histology

Adenosine triphosphatase staining at pH 9.6 on muscle fibers from untrained canine latissimus dorsi obtained from normal controls revealed approximately 50% to be



A

B

Fig 10. Comparison of latissimus dorsi adenosine triphosphatase stains after 3 months of stimulation (A) and after 3 months without stimulation (B). Essentially 100% of stimulated fibers were converted to lighter-staining type I slow-twitch fibers.

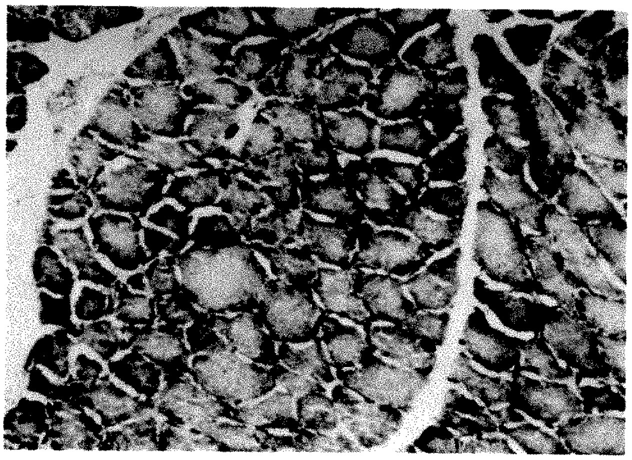


Fig 11. Nicotinamide adenine dinucleotide (reduced form) stain of stimulated muscle after 3 months documenting absence of damage at cellular level.

type II and 50% to be type I (Fig 9). All 10 experimental animals had essentially 100% conversion of type II to type I fibers on the stimulated side after 3 months of pacing. Figure 10A shows the typical pattern observed. No histologic differences were detected when muscles trained with a 360-degree electrode were compared with those trained with a 180-degree electrode. All unstimulated (control) latissimus dorsi samples showed no change in distribution of type II or type I fibers by adenosine triphosphatase staining at pH 9.6 (see Fig 10B).

Nicotinamide adenine dinucleotide (reduced form) staining for each latissimus dorsi muscle whether unstimulated or stimulated was performed at the time of sacrifice after strength-duration curves had been completed. No evidence of muscle degeneration was found in any biopsy specimen, and all specimens became uniformly stained with NADH. A typical NADH stain for stimulated muscle after 3 months is shown in Figure 11.

Samples of each nerve at the level of the nerve cuff electrode were also sent for histologic analysis. Figures 12A and 12B show samples of typical control and stimulated nerve. There is no evidence of axonal degeneration or damage to perineurium.

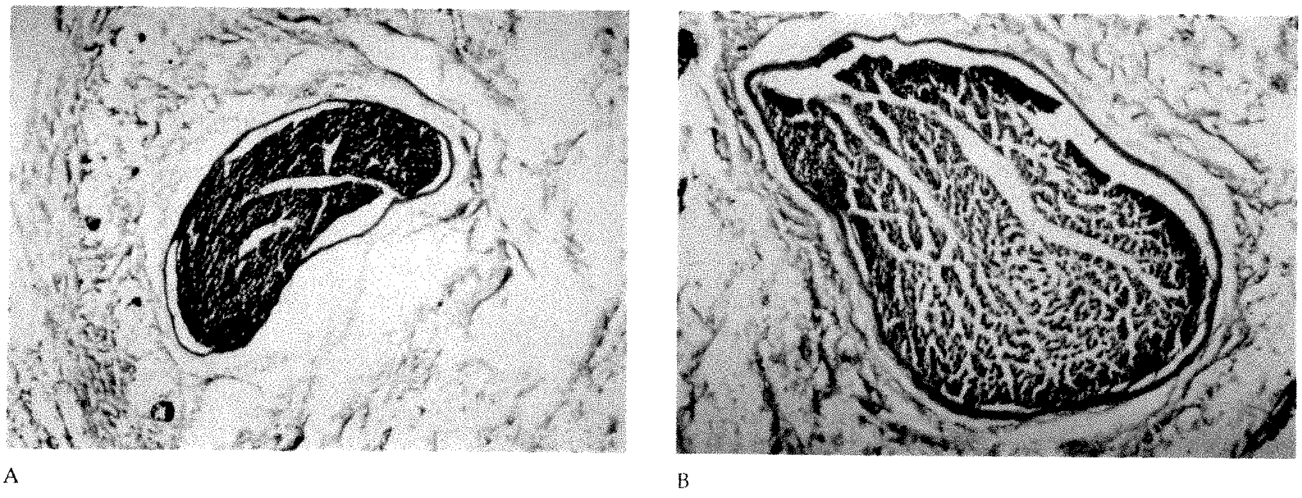
Complications

Three animals did not complete the study. The first had a 180-degree nerve cuff electrode on the unstimulated side that was infected at the time of sacrifice. The second had a fractured 360-degree nerve cuff electrode on the unstimulated side at the junction of the cuff and lead as well as a wound infection. The third animal had an atrophied latissimus dorsi without evidence of any nerve tissue within an intact 360-degree nerve cuff electrode on the unstimulated (control) side. Nerve and muscle degeneration in this third animal was attributed to compression by the 360-degree nerve cuff electrode.

Comment

Multiple experimental and clinical efforts are underway using skeletal muscle for cardiac assistance. These include efforts at creation of a skeletal muscle ventricle in animals, extraaortic counterpulsation devices in animals, and cardiomyoplasty in humans. Clinically, these studies have used an intramuscular electrode for stimulation of skeletal muscle. An alternate method of skeletal muscle stimulation (which has been used experimentally for the creation of skeletal muscle ventricles) is the nerve cuff electrode [8]. A 180-degree (half-cuff) electrode has been used extremely successfully in diaphragm pacing, where it has a particularly long clinical follow-up with excellent results. These nerve cuff electrodes have been shown to be safe and effective for diaphragm pacing in quadriplegics and in patients with central alveolar hypoventilation [9].

Our evaluation of two nerve cuff electrode configurations (180-degree and 360-degree) demonstrates the nerve cuff electrode to be safe for chronic stimulation of canine latissimus dorsi. All nerve cuffs placed for stimulation (180-degree and 360-degree) functioned without problem. Although cuff dislodgement with stimulation might be expected, it did not occur. Dislodgement was prevented by affixing the nerve cuff to the surrounding tissues with several sutures and avoidance of premature (earlier than 1 to 2 weeks) skeletal muscle stimulation. At the time of sacrifice, all electrodes were covered by fibrous tissue, and the thoracodorsal nerve, electrode, and underlying latissimus dorsi muscle moved as a unit.



A B

Fig 12. Luxol fast blue stain of unstimulated (A) and stimulated (B) thoracodorsal nerve documenting absence of damage to either.

Nerve cuff electrode stimulation was extremely effective for conditioning of canine skeletal muscle. Essentially 100% conversion of type II to type I fibers was noted in all muscles by adenosine triphosphatase staining. No evidence of cellular muscular damage was detected with NADH staining. As opposed to electrodes that are weaved through muscular tissue, the nerve cuff electrode results in extremely effective fiber recruitment because all branches of the thoracodorsal nerve are stimulated. Furnary and colleagues [10] have reported improved efficiency of the nerve cuff electrode over those woven through muscular tissue, consistent with our findings. Nerve cuff electrodes may be an important way to maximize nerve fiber recruitment and thus maximize the strength of latissimus dorsi contraction. In addition, work by Thoma and associates [11] has shown direct nerve stimulation to be effective for skeletal muscle stimulation.

Electrical studies using strength-duration curves revealed the nerve cuff electrode to have threshold voltages and threshold currents (at the commonly used pulse widths of 150 to 250 microseconds) well within the range of commonly used cardiomyostimulators. These thresholds, approximately 0.4 to 0.6 V, allow a large safety margin (because cardiomyostimulator output up to 10 V is feasible) and can be expected to extend generator life.

The increases in threshold voltage and current over time, with both the 180-degree nerve cuff electrode and the 360-degree nerve cuff electrode, are similar to the increases seen in cardiac pacing and phrenic pacing. In cardiac pacing, thresholds plateau at 3 to 6 months, an interval similar to that in the present study [12]. Long-term measurements of threshold voltage and current in human phrenic nerve have shown very stable threshold values over 15 years [13]. A limited study of a similar nerve cuff electrode applied to the thoracodorsal nerve showed the increase in threshold to peak at 6 months in the canine model, although the electrode configuration was not specified [14]. Longer term studies will be necessary before plateau values for threshold voltage and current for chronic skeletal muscle stimulation can be completely documented.

Initially, we believed the 360-degree configuration might offer more efficient stimulation of the thoracodorsal nerve. However, our electrical studies do not bear this out. Although there is a tendency for the 360-degree configuration to have lower threshold voltages and currents, there is no statistically significant difference between it and the 180-degree nerve cuff electrode and no difference of any practical significance. This finding is similar to studies in diaphragmatic pacing, in which 180-degree nerve cuff electrodes have been found to be as efficient as the 360-degree nerve cuff electrodes. In other respects, (nerve histology, fiber conversion, and lack of muscle damage) there is no appreciable difference between the two configurations of electrodes.

Nevertheless, in 1 case an unstimulated control 360-degree nerve cuff electrode was believed to have compressed the thoracodorsal nerve resulting in its degeneration. This complication has been noted in diaphragm pacing [15]. Although it is not definite that this nerve degeneration was caused by the nerve cuff electrode, this laboratory experience and our clinical experience with phrenic pacing leads us to prefer the 180-degree configuration, which avoids the potentially damaging circumferential entrapment of the nerve by fibrous tissue.

We conclude that the two configurations of electrode are both effective for transformation and chronic stimulation of canine latissimus dorsi. There is no electrical advantage of a 360-degree configuration over a 180-degree configuration; nor is there any advantage in terms of histologic transformation or preservation of myocyte integrity. However our clinical experience in diaphragm pacing and the one experimental instance of nerve degeneration with the 360-degree electrode in the present study lead us to prefer the 180-degree nerve cuff.

We acknowledge the contributions of our statistician, Terry O'Connor, MPH, Department of Anesthesia, Yale University.

References

1. Anderson DR, Pochettino A, Hammond RL, et al. Autogenously lined skeletal muscle ventricles in circulation. J Thorac Cardiovasc Surg 1991;101:661–70.
2. Acker MA, Hammond RL, Mannion JD, et al. Skeletal muscle as the potential power source for a cardiovascular pump: assessment in vivo. Science 1989;236:324–7.
3. Carpentier A, Chacques JC. Myocardial substitution with a stimulated skeletal muscle: first successful clinical case. Lancet 1985;1:1267.
4. Rossi MA, Braile DM, Souza DRS, et al. Dynamic cardiomyoplasty in chronic Chagas' heart disease: clinicopathologic data. Ann Thorac Surg 1991;51:649–51.
5. Lee P, Stokes K, Malek A, et al. Threshold and impedance measurements of steroid and nonsteroid cuff electrodes. In: Chiu RC-J, Bourgeois J, eds. Transformed muscle for cardiac assist and repair. Mount Kisco, NY: Futura, 1990:267–80.
6. Glenn WWL, Hogan JF, Loke J, et al. Ventilatory support by pacing of the conditioned diaphragm in quadraplegia. N Engl J Med 1984;310:1150–5.
7. Dubowitz V, Brooke MH. Muscle biopsy: a modern approach. Major problems in neurology. Vol II. Philadelphia: Saunders, 1973:27–33.
8. Acker MA, Hammond RL, Mannion JD, et al. An autologous biologic pump motor. J Thorac Cardiovasc Surg 1986;92: 733–46.
9. Glenn WWL, Phelps MH, Elefteriades JA, et al. Twenty years of experience in phrenic nerve stimulation to pace the diaphragm. PACE 1986;9:780–4.
10. Furnary AP, Trumble DR, Vu TQ, et al. Perineural leads and burst stimulation optimize contraction of skeletal muscle. ASAIO Trans 1991;37:M164–6.
11. Thoma HT, Frey M, Girsch W, et al. First experimental application of multichannel stimulation devices for cardiomyoplasty. J Cardiac Surg 1991;6(Suppl):252–8.
12. Furman S. Cardiac pacing and pacemakers. In: Glenn WWL, Baue AE, Geha AS, Hammond GL, Laks H, eds. Thoracic And Cardiovascular Surgery, 4th ed. Norwalk, CT: Appleton-Century-Crofts, 1983:1228–75.
13. Elefteriades JA, Hogan JF, Handler A, et al. Long-term follow-up of bilateral diaphragm pacing in quadriplegia [Letter]. N Engl J Med 1992;326:1433–4.
14. Hohenhaus E, Anderson WA, Pochettino A, et al. Skeletal muscle for cardiac assistance. In: Kron I, Mavroudis C, eds. Cardiac surgery: state of the art reviews. Vol 4, No 3. Philadelphia: Hanley & Belfus, 1990:677–701.
15. Kim JK, Manuelides EE, Glenn WWL, et al. Light and electron microscopic studies of phrenic nerves after long-term electrical stimulation. J Neurosurg 1983;58:84–91.

Technique of Open Distal Anastomosis for Repair of Descending Thoracic Aortic Aneurysms

Denton A. Cooley, MD, and Robert T. Baldwin, MD

Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas

Ischemic injury to the spinal cord and kidneys continues to be the major complication after resection of aneurysms involving the descending and proximal abdominal aorta. Our recent surgical experience with use of *only* a proximal clamp on the aorta to perform an "open" distal anastomosis has proved this technique to be safe and expeditious. We therefore compared our results using the technique of open distal anastomosis for aneurysm repair with those of the conventional two-clamp technique. Since January 1989, we have used the conventional two-clamp technique in 31 patients (group 1) and the technique of open distal anastomosis in 24 patients (group 2). No significant differences were noted between the two groups in terms of age, sex, cause of aneurysm, extent of aneurysm, or site of proximal cross-clamp. The average distal ischemic time was 31 minutes in group 1 patients and 26 minutes in group 2 patients. Renal insufficiency occurred in 8 of 31 patients in group 1 and in 0 of 24 patients in group 2 ($p = 0.01$). Neurologic complications occurred in 4 patients in group 1 and in 1 patient in group 2. Early mortality rates were similar for both groups (4 of 31 [13%], group 1; 4 of 24 [17%], group 2). Deaths were attributed to multiorgan failure and sepsis in 6 patients and coexisting coronary artery disease in 2 patients. Based on these results, we believe the technique of open distal anastomosis is safe and may improve the outcome in patients undergoing operation for descending thoracic aneurysms. Maintaining the distal circulation during aortic cross-clamping does not appear to be necessary in this experience.

(Ann Thorac Surg 1992;54:932–6)

The results obtained with resection and repair of aneurysms involving the descending thoracic aorta have improved during the past four decades; however, the ischemic complications related to aortic cross-clamping continue to result in devastating postoperative morbidity. Renal failure and paraplegia were noted in the earliest series of patients undergoing descending thoracic aortic aneurysm resection [1–3], and they remain the two most frequent major complications [4–8].

Since these initial reports, hundreds of investigators have attempted to explain the mechanism of ischemic injury to the spinal cord and to develop methods to prevent the occurrence of postoperative paraplegia and paraparesis. The conventional belief has been that by keeping an increased abdominal aortic pressure capable of maintaining the distal circulation during aneurysm resection, the incidence of paraplegia would be decreased. Because of our recent experience, however, we are now reevaluating this concept.

During a difficult technical operation to repair a descending thoracic aortic aneurysm, we found it impossible to place a distal clamp across the aorta below an aneurysm that had extended to the level of the aortic hiatus. To avoid repositioning for a thoracoabdominal incision, an "open," unclamped distal anastomosis was performed to the supraceliac aorta without the need for further surgical exposure.

Encouraged by the absence of neurologic complications associated with this technique, we increased its application. This review was undertaken to compare our results using the technique of open anastomosis with those of the conventional two-clamp technique for distal aneurysm repair.

Patients and Methods

From January 1989 to June 1991, 55 consecutive patients underwent resection and graft replacement of aneurysms involving either the descending thoracic aorta or thoracoabdominal aorta at the Texas Heart Institute in Houston. Of those patients, 31 underwent aneurysm repair with the conventional two-clamp technique (group 1) and 24 underwent repair with the open distal anastomosis technique (group 2).

A retrospective review of the patients' postoperative outcomes was undertaken by using their hospital records and clinic files. Data were recorded for patient information (demographics, past medical history), aneurysmal characteristics (extent, location, cause, presence of aortic rupture), intraoperative details (aortic cross-clamp time, level of proximal aortic cross-clamp, intercostal vessel reattachment), and postoperative outcome (neurologic changes after operation, renal failure requiring dialysis, postoperative hemorrhage requiring reexploration, and 30-day mortality).

The surgical technique was standardized for each group and differed only in the method of managing the distal anastomosis. The same surgeon (D.A.C.) performed all

---

Accepted for publication March 12, 1992.

Address reprint requests to Dr Cooley, Texas Heart Institute, PO Box 20345, Houston, TX 77225.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

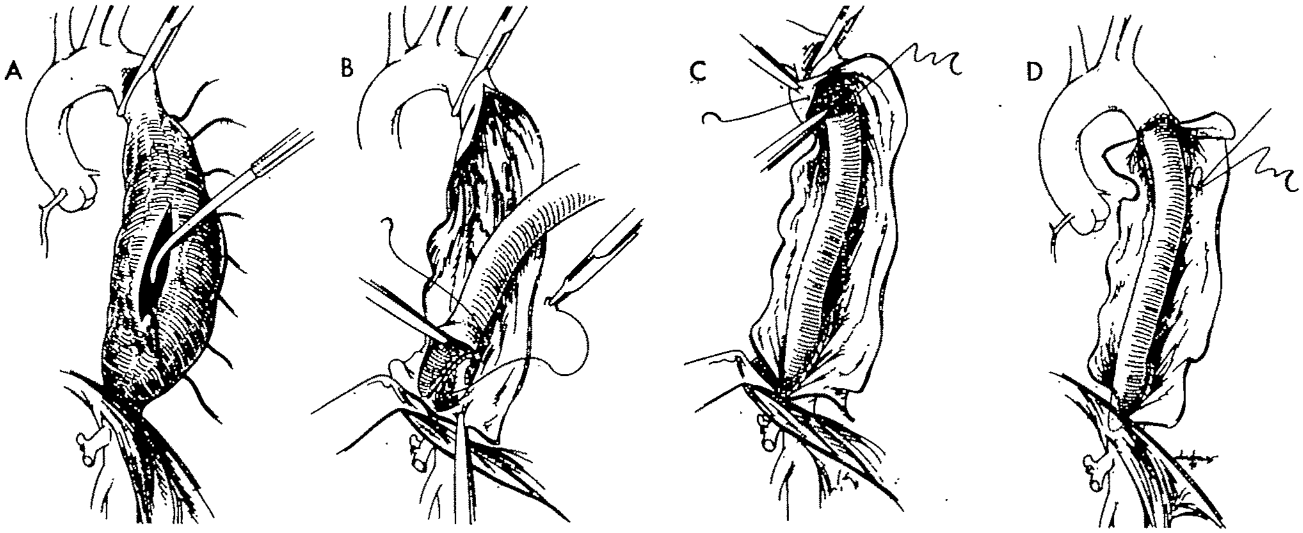


Fig 1. The distal anastomosis is performed without an aortic clamp. Continuous aspiration of blood to the autotransfusion reservoir maintains a clear operative field.

operations, and the intraoperative anesthetic care was standardized. Thiopental sodium was intravenously administered for induction of anesthesia, and a narcotic with inhaled isoflurane was used for maintenance. A sodium nitroprusside infusion was used as needed during proximal aortic cross-clamping for blood pressure control and was tapered before release of the clamp. Hypotension during operation or in the postoperative period was treated aggressively in all cases.

The outcome of patients who underwent aneurysmal repair by way of the conventional technique (group 1) was compared with those who underwent resection by use of the open distal anastomosis (group 2). The choice of surgical technique was that of the surgeon and was not influenced by patient or aneurysmal characteristics. The surgical technique, however, did reflect the time during which the operation was performed. Early in 1989, for example, most patients underwent resection by the conventional technique, whereas by 1991, almost all patients underwent repair by the open technique of distal anastomosis.

Statistical Analysis

Univariate tests were performed to compare the two groups by use of Student's t test, Fisher's exact test, or χ^2 analysis as appropriate. A p value of less than 0.05 was considered significant for all statistical calculations. Continuous data are presented as the mean ± the standard deviation.

Technique of "Open" Distal Anastomosis

Generally, an endotracheal tube is used to administer anesthesia; however, in cases involving extensive lesions, an endobronchial tube is substituted to provide selective right lung ventilation. A standard left posterolateral skin incision is made, and the chest is entered through the fourth intercostal space to establish access to the proximal portion of the descending aorta. For extensive aneurysms, the seventh intercostal space may be entered as well to expose the distal extent of the aneurysm. Thoracoabdominal and suprarenal aortic aneurysms require a formal thoracoabdominal incision.

The aorta is dissected at the site of the proximal clamp, and heparin (1 mg/kg body weight) is given systemically. The clamp is then applied, and the aneurysm is incised longitudinally. The intraluminal thrombus is quickly removed and any atheromatous debris removed from the sites of anastomosis. Blood is aspirated continuously through the autotransfusion device and returned to the patient. No attempt is made to control bleeding from the distal aorta or from the segmental vessels exposed within the aneurysmal lumen (Fig 1).

A woven Dacron tube graft of the appropriate size is then anastomosed to the distal aorta by using 2-0 polypropylene sutures. To expedite the anastomosis, a large MH double-armed needle (No. 8853H; Ethicon, Somerville, NJ) is used (Fig 2). Whenever possible, an oblique suture line is fashioned to incorporate any back-bleeding segmental vessels into the new lumen. This allows for preservation of intercostal flow and alleviates the need to reattach vessels individually.

When the distal anastomosis is complete, the graft is attached to the proximal aorta by use of 2-0 or 3-0 polypropylene suture. The proximal clamp is released gradually while appropriate pharmacologic agents are administered to provide a stable proximal blood pressure. Finally, the segmental vessels are oversewn as circulatory stability is restored. The remaining aneurysm is tailored and sewn over the Dacron graft. The effect of heparin is reversed with protamine sulfate. The left lung is reexpanded, and the incision is closed. Conventional chest tube drainage is used. All of the aspirated blood is autotransfused after processing.

The open technique described here is also used to repair thoracoabdominal aneurysms. A single patch containing the superior mesenteric, celiac, and both renal arteries is

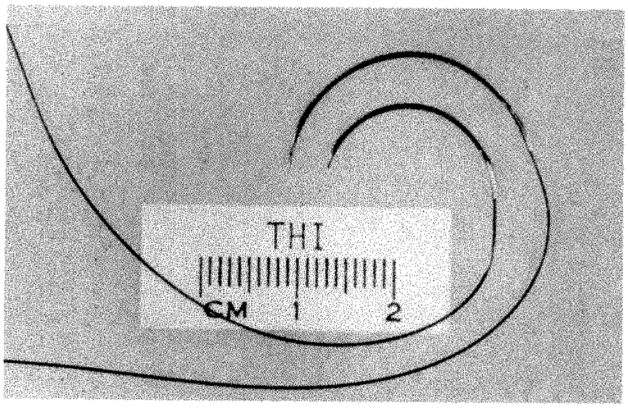


Fig 2. Large MH needle adjacent to the standard SH needle. The MH needle is preferred for a more expeditious anastomosis.

reattached after the open distal anastomosis is completed. The proximal anastomosis is then completed, and flow is restored to the distal circulation. Control of the segmental vessels, tailoring of the aneurysmal wall, and closing of the incision are done in a fashion similar to that described for descending aneurysms.

Results

The patient demographics and past medical history were similar in both groups. The mean age of the group 1 patients (57 years) was not statistically different from that of the group 2 patients (61 years). The predominance of males of 3.4:1 in group 1 (24 of 31 patients, 77%) was similar to that of 2.4:1 in group 2 (17 of 24 patients, 71%). Concomitant hypertension, chronic obstructive pulmonary disease, a history of previous cardiac operation, and a history of previous aneurysm operation were frequent in both groups (Table 1).

There were no sizable differences between the two groups in terms of the characteristics of the aneurysms. In both groups, atherosclerosis was the most frequent underlying cause of the aneurysms (19 in group 1; 17 in group 2). Chronic dissection was the second most frequent cause (9 in group 1; 7 in group 2). Posttraumatic aneurysm formation at the aortic isthmus occurred in 3 patients in group 1.

Extent and location of aneurysms varied slightly, with more extensive aneurysms occurring in patients who underwent repair by the open technique (Table 2). For example, larger aneurysms covering the entire descending thoracic aorta occurred more frequently in group 2 than in group 1 patients. Aneurysms confined to the proximal descending thoracic aorta were more common in group 1. Thoracoabdominal aneurysms were slightly more common in group 1 than in group 2 patients. The incidence of a contained rupture was similar for both groups.

Table 1. Patient History

Patient Group[a]	Hypertension	COPD	Previous Cardiac Operation	Previous Aneurysm Operation
Group 1	16	5	12	7
Group 2	15	9	8	4

[a] Group 1 patients underwent aneurysm repair with the conventional two-clamp technique. Group 2 patients underwent aneurysm repair with open distal anastomosis.

COPD = chronic obstructive pulmonary disease.

Table 2. Site of Aneurysms

Patient Group	DTA			TAA
	Proximal	Distal	Entire	
Group 1	11	0	9	11
Group 2	2	1	15	6

DTA = descending thoracic aorta; TAA = thoracoabdominal aorta.

The intraoperative variables associated with aneurysm resection were similar for both groups. The proximal aortic clamp was located between the left common carotid and left subclavian arteries in 13 of 31 patients (42%) in group 1 and in 8 of 24 patients (33%) in group 2. The clamp was placed on the proximal descending aorta in 8 of 31 patients (26%) in group 1 and 10 of 24 patients (42%) in group 2. In the remaining patients, the proximal clamp was placed in the mid or distal descending thoracic aorta. Aortic occlusion times were longer in group 1 (31 ± 5 minutes) than in group 2 patients (26 ± 4 minutes), but the difference was not statistically significant ($p = 0.10$). Intercostal vessels were incorporated into the new lumen by an oblique anastomosis whenever possible regardless of the selected procedure; individual reattachment of intercostal vessels was not done in either group. In all patients with thoracoabdominal aneurysms, we used a single Carrel patch to incorporate the renal and visceral arteries. The use of heparin (1 mg/kg body weight administered intravenously) was the same for both groups.

There was no significant difference in early mortality rates (30 days postoperatively) between the two groups (4 of 31 [13%], group 1; 4 of 24 [17%], group 2). All four deaths in group 1 were caused by multiorgan failure and sepsis. The four deaths in group 2 were attributed to multiorgan failure and sepsis (2) and coexisting coronary artery occlusive disease (2).

Spinal cord injury occurred less frequently in group 2 (1 of 24, 4%) than in group 1 (4 of 31, 13%), but the difference was not statistically significant. The only case of paraplegia in group 2 was in a 69-year-old man who had undergone infrarenal aneurysm resection several years before this admission. Only 1 patient in group 1 underwent thoracoabdominal aneurysm replacement. All 5 patients in whom paraplegia developed in this series had aortic clamp times of 30 minutes or greater.

Renal failure requiring dialysis was not seen in any (0 of 24) patients in group 2, but was seen with a disturbing frequency (8 of 31, 26%) in group 1 ($p = 0.01$). Five of the 8 patients in whom renal failure developed had undergone resection of extensive atherosclerotic thoracoabdominal aneurysms. Of the patients having nonthoracoabdominal involvement, those in group 2 had a lower incidence of renal failure (0 of 18) than those in group 1 (3 of 20). Two of the 8 patients with renal failure had aortic clamp times of less than 30 minutes, whereas the other 6 patients had clamp times ranging from 30 to 60 minutes.

Postoperative hemorrhage requiring reoperation occurred less frequently in group 2 (3 of 24) than in group 1 (5 of 31), but the difference was not statistically significant. Other sporadic complications included vocal nerve paralysis (2 patients), wound dehiscence (2 patients), and stroke (1 patient), but neither group showed a predilection toward these complications.

Comment

The decrease in ischemic complications related to aortic cross-clamping noted in the patients in whom the open distal anastomosis technique was used may be related to the shorter distal ischemic times in that group. Lengthy aortic occlusion times have consistently been shown to increase the incidence of paraplegia and renal failure [4, 9, 10]. Aortic occlusion times in excess of 30 minutes have correlated with a marked increase in the incidence of paraplegia [4, 9]. Although the difference in clamp times in our study between those in whom the open anastomosis was used (26 minutes) and those in whom conventional repair was performed (31 minutes) seems small, this small difference may represent a critical level of spinal ischemic tolerance.

The relative protection from ischemic spinal cord injury seen in our patients who underwent procedures with use of open anastomosis creates a challenge to the conventional belief that favors shunting or bypass to augment abdominal aortic pressure [7–9, 11–13]. Improved results with use of an open distal anastomosis that effectively lowers the abdominal aortic pressure to zero underscores the poor correlation between distal aortic pressure and spinal cord blood flow. This may be due to the location of the anterior spinal artery and its dependency on the arteria radicularis magna, which usually originates above the abdominal aorta [10, 14, 15]. At the level of the potential injury, the individual radicular arteries contribute to spinal cord perfusion. This local radicular arterial pressure may not, however, correlate with either the distal aortic pressure or the intercostal artery pressure in an adult human spinal cord that depends on a noncontinuous anterior spinal artery and diseased vessels for its vascular supply. The diminished enthusiasm for shunting [4–6, 16, 17] may, in part, be a result of this phenomenon.

Equally important to the local arterial pressure in spinal cord perfusion is the local venous pressure. In our early studies of aortic cross-clamping in dogs, the cerebrospinal fluid (CSF) pressure was noted to rise immediately on cross-clamping and then fall, even though the proximal systemic arterial pressure was elevated [18, 19]. These studies led to the conclusion that the CSF pressure reflects the local venous pressure and that a reduction in CSF pressure (by subarachnoid aspiration or a urea-induced diuresis) provides a sufficient perfusion gradient between the local spinal radicular arteries and the local spinal venous return to maintain arterial flow into the cord substance, despite critically low pressure in the abdominal aorta [18, 19]. In several patients who underwent aneurysm resection by use of the open technique with continuous central venous and CSF pressure monitoring, it has been noted that CSF pressure increases with cross-clamping, but decreases to low levels after the aneurysm has been opened and the abdominal aorta decompressed. It is possible, therefore, that allowing the intercostal and lumbar vessels to drain during the open anastomosis reduces the CSF pressure, thereby increasing blood flow to the spinal cord substance and contributing to spinal cord protection. Studies in dogs and humans have confirmed that preoperative CSF drainage has a protective effect against ischemic spinal cord injury during resection of aneurysms of the descending thoracic aorta [20–24].

Investigators have developed adjuncts to minimize spinal cord ischemia, including hypothermia [25, 26], localization of the arteria radicularis magna [10, 27, 28], and intraoperative somatosensory [8, 27] and motor-evoked potentials [10, 29]. In our experience, however, the factor that consistently relates to decreased mortality and morbidity is a short aortic clamp time. In another review of our cases, Livesay and associates [4] found that the duration of aortic occlusion was the most important factor in minimizing the risk of paraplegia (more than age, extent of the lesion, and rupture). They concluded that the risk of paraplegia would be minimal if surgeons limited cross-clamp time to 30 minutes. In an effort to minimize clamp times with the open technique of anastomosis, use of a large MH needle has been helpful to expedite the open distal anastomosis. In addition, performing an open anastomosis makes the false lumen easier to repair in dissecting aneurysms and minimizes the risks of clamp atheroembolism and clamp trauma [30].

We believe that the open technique for resecting aneurysms involving the descending thoracic aorta is safe and may offer some protection against postoperative spinal cord and renal ischemic injuries. Because good results have been achieved with a distal aortic pressure of zero, the role of shunting and partial cardiopulmonary bypass in spinal cord protection may need to be reevaluated.

References

1. Cooley DA, DeBakey ME. Surgical considerations of intrathoracic aneurysms of the aorta and great vessels. Ann Surg 1952;135:660–80.
2. DeBakey ME, Cooley DA. Successful resection of aneurysm of thoracic aorta and replacement by graft. JAMA 1953;152:673–6.
3. Cooley DA, DeBakey ME. Surgical considerations of excisional therapy for aortic aneurysms. Surgery 1953;34:1005–20.
4. Livesay JJ, Cooley DA, Ventemiglia R, et al. Surgical experience in descending thoracic aneurysmectomy with and without adjuncts to avoid ischemia. Ann Thorac Surg 1985;39:37–46.
5. Crawford ES, Walker HSJ, Saleh SA, Normann NA. Graft replacement of aneurysm in descending thoracic aorta: results without bypass or shunting. Surgery 1981;89:73–85.
6. Najafi H, Javid H, Hunter J, Serry C, Monson D. Descending aortic aneurysmectomy without adjuncts to avoid ischemia. Ann Thorac Surg 1980;30:326–35.

7. Cunningham JN, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta. Ann Surg 1982;196:285–96.
8. Laschinger JC, Izumoto H, Kouchoukos NT. Evolving concepts in prevention of spinal cord injury during operations on the descending aorta. Ann Thorac Surg 1987;44:667–74.
9. Katz NM, Blackstone EH, Kirklin JW, Karp RB. Incremental risk factors for spinal cord injury following operation for acute traumatic aortic transection. J Thorac Cardiovasc Surg 1981;81:669–74.
10. Svensson LG, Patel V, Robinson MF, Ueda T, Roehm JOF, Crawford ES. Influence of preservation or perfusion of intraoperatively identified spinal cord blood supply on spinal motor evoked potentials and paraplegia after aortic surgery. J Vasc Surg 1991;13:355–65.
11. Cooley DA, DeBakey ME, Morris GL. Controlled extracorporeal circulation in surgical treatment of aortic aneurysms. Ann Surg 1957;146:473–86.
12. Borst HG. Occlusion of intercostal and lumbar aortic branches using plastic plugs. Ann Thorac Surg 1987;44:91.
13. Laschinger JC, Cunningham JN, Nathan IM, Knopp EA, Cooper MM, Spencer FC. Experimental and clinical assessment of the adequacy of partial bypass in maintenance of spinal cord blood flow during operations on the thoracic aorta. Ann Thorac Surg 1983;36:417–28.
14. Svensson LG, Rickards E, Coull A, Rogers G, Fimmel CJ, Hinder RA. Relationship of spinal cord blood flow to vascular anatomy during thoracic aortic cross-clamping and shunting. J Thorac Cardiovasc Surg 1986;91:71–8.
15. Wadouh F, Lindemann EM, Arndt CF, Hetzer R, Borst HG. The arteria radicularis magna anterior as a decisive factor influencing spinal cord damage during aortic occlusion. J Thorac Cardiovasc Surg 1984;88:1–10.
16. Crawford ES, Rubio PA. Reappraisal of adjuncts to avoid ischemia in the treatment of aneurysms of descending thoracic aorta. J Thorac Cardiovasc Surg 1973;66:693–704.
17. Crawford ES, Mizrahi EM, Hess KR, Coselli JS, Safi HJ, Patel V. The impact of distal aortic perfusion and somatosensory evoked potential monitoring on prevention of paraplegia after aortic aneurysm operation. J Thorac Cardiovasc Surg 1988;95:357–67.
18. Blaisdell FW, Cooley DA. Relationship of spinal fluid pressure and incidence of paraplegia following temporary aortic occlusion: an experimental study. Surg Forum 1960;11:153–4.
19. Blaisdell FW, Cooley DA. The mechanism of paraplegia after temporary thoracic aortic occlusion and its relationship to spinal fluid pressure. Surgery 1962;51:351–5.
20. Berendes JN, Bredee JJ, Schipperheyn JJ, Mashour YAS. Mechanisms of spinal cord injury after cross-clamping of the descending thoracic aorta. Circulation 1982;66(Suppl 1):112–6.
21. Symbas PN, Pfaender LM, Drucker MH, Lester JL, Gravanis MB, Zacharopoulos L. Cross-clamping of the descending aorta. J Thorac Cardiovasc Surg 1983;35:300–5.
22. Oka Y, Miyamoto T. Prevention of spinal cord injury after cross-clamping of the thoracic aorta. Jpn J Surg 1984;15:159–62.
23. McCullough JL, Hollier LH, Nugent M. Paraplegia after thoracic aortic occlusion: influence of cerebrospinal fluid drainage. J Vasc Surg 1988;1:153–60.
24. Bower TC, Murray MJ, Gloviczki P, Yaksh TL, Hollier LH, Pairolero PC. Effects of thoracic aortic occlusion and cerebrospinal fluid drainage on regional spinal cord blood flow in dogs: correlation with neurologic outcome. J Vasc Surg 1989;9:135–44.
25. Pontius RG, Brockman HL, Hardy EG, Cooley DA, DeBakey ME. The use of hypothermia in the prevention of paraplegia following temporary aortic occlusion: experimental observations. Surgery 1954;36:33–8.
26. Colon R, Frazier OH, Cooley DA, McAllister HA. Hypothermic regional perfusion for protection of the spinal cord during periods of ischemia. Ann Thorac Surg 1987;43:639–43.
27. Laschinger JC, Cunningham JN, Nathan IM, Krieger K, Isom OW, Spencer FC. Intraoperative identification of vessels critical to spinal cord blood supply—use of somatosensory evoked potentials. Curr Surg 1984;41:107–9.
28. Laschinger JC, Cunningham JN, Cooper MM, Baumann FG, Spencer FC. Monitoring of somatosensory evoked potentials during surgical procedures on the thoracoabdominal aorta. J Thorac Cardiovasc Surg 1987;94:260–5.
29. Elmore JR, Gloviczki P, Harper CM, et al. Failure of motor evoked potentials to predict neurologic outcome in experimental thoracic aortic occlusion. J Vasc Surg 1991;14:131–9.
30. Cooley DA, Livesay JJ. Technique of "open" distal anastomosis for ascending and transverse arch resection. Cardiovasc Dis 1981;8:421–6.

Expanding Wire Stents in Benign Tracheobronchial Disease: Indications and Complications

Samer A. M. Nashef, FRCS, Claire Dromer, MD, Jean-François Velly, MD,
Louis Labrousse, MD, and Louis Couraud, MD

Department of Thoracic Surgery, Xavier Arnozan Hospital, Pessac, France

Prosthetic tracheobronchial stents provide palliative treatment for narrowed airways where surgical resection is inadvisable. Over a 1-year period, 28 Gianturco expanding wire stents were used in 15 patients for nonneoplastic indications: pure fibrous airway stenosis (6), fibroinflammatory stenosis (4), and tracheobronchial malacia (5). Insertion was technically straightforward. A satisfactory airway lumen with immediate improvement in ventilatory function was obtained in all patients. After insertion all patients had an irritation-type cough that either subsided spontaneously (10 patients) or was successfully suppressed with inhaled corticosteroid therapy (5 patients). The most common complication (12 patients) was granuloma formation leading to stent removal in 3 patients with fibroinflammatory stenosis. Other complications were dysphagia (1), suction catheter entrapment (1), and fatal massive hemoptysis (1). At a mean follow-up of 13 months (range, 3 to 19 months) all remaining stents are functioning well with no displacement or infection. Overall results were satisfactory in pure fibrous stenoses and tracheobronchial malacia but poor in the presence of inflammation. Tracheobronchial wire stents can be successfully used in selected patients.

(Ann Thorac Surg 1992;54:937–40)

The treatment of choice for airway stenosis is surgical resection with end-to-end anastomosis. In many cases this may not be feasible because of the site and extent of the stenosis, the cause of the underlying disease, and the general state of the patient. Tracheobronchial malacia, on the other hand, is not amenable to surgical correction. Nonsurgical palliative methods have been developed to deal with airway stenosis and include laser photocoagulation and several types of endoprostheses: Montgomery T tubes can be used in high tracheal or laryngotracheal stenoses but require a tracheostomy; simple silicone tubes can be used in lower, bronchial stenoses. Both of these tubes interfere with airway mucociliary function, and simple tubes cannot be easily placed in the right main bronchus without obstructing the orifice of the upper lobe. These limitations have led to a recent interest in expanding wire stents such as the Gianturco stent, which had already been used in vascular and biliary pathology [1–3]. Experimental work has confirmed that such stents can be used in the tracheobronchial tree [4–6]. We describe our experience with Gianturco stents in patients with airway luminal narrowing due to nonneoplastic disease.

Patients and Methods

The Gianturco stent (Cook Inc) consists of a continuous loop of stainless steel zigzag wire which is compressed into a narrow cylinder and therefore capable of expansion on delivery (Fig 1). The wire is barbed on its external aspect to allow anchorage at the desired intraluminal position. The stent is presented precompressed within a sterile cartridge, which is 10 cm long but only 0.4 cm in diameter. It is available in single and double postexpansion lengths (2.5 and 5 cm) and three diameters (1.5, 2, and 3 cm). An introducer sheath and obturator are provided to facilitate implantation.

The stent is implanted with the patient under general anesthesia. Using a rigid bronchoscope, bronchial toilet is performed and the lesion in question is assessed. Any associated granulomata can be dealt with using laser photocoagulation. The sheath is then inserted within the bronchoscope so that its distal end is precisely at the level of the upper border of the lesion to be stented. The cartridge containing the stent is placed end-to-end at the proximal end of the sheath. The obturator is then used to push the stent out of its cartridge, into the sheath, and through the sheath to its distal end where it is extruded to lie within the narrowed airway. The sheath is then removed and the satisfactory positioning of the stent confirmed using the bronchoscope. Other stents, if required, can be placed using the same technique.

Over a 1-year period 28 Gianturco stents were inserted in 15 patients with nonneoplastic airway narrowing. Mean age was 55 years (range, 25 to 80 years) and 6 patients were female. The number of stents per patient ranged between one and four (Fig 2). Lesions were pure fibrous stenosis in 6 patients, fibroinflammatory stenosis in 4 patients, and tracheobronchial malacia in 5 patients. Indications, stent number, and position are detailed in Table 1.

All patients had operative antibiotic cover. Nebulized inhalations including corticosteroids were continued for 5

Accepted for publication March 19, 1992.

Address reprint requests to Dr Couraud, Service de Chirurgie Thoracique, Hôpital Xavier Arnozan, 33604 Pessac, France.

© 1992 by The Society of Thoracic Surgeons

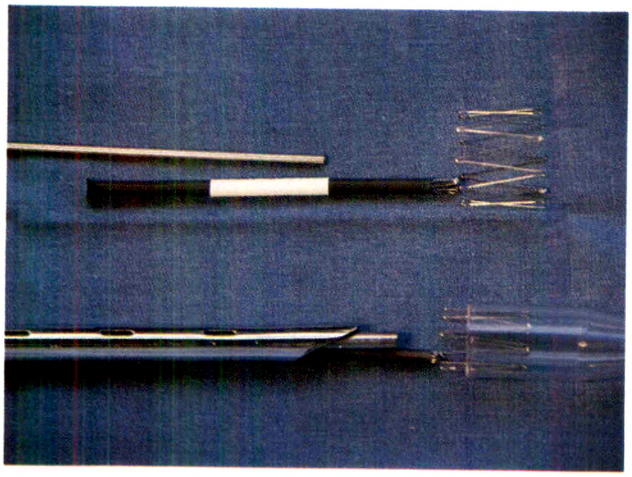


Fig 1. Two stents, one precompressed stent within its cartridge alongside expanded stent (top) and a similar arrangement within the rigid bronchoscope and a transparent model of an airway (bottom).

postoperative days. All patients had at least one follow-up endoscopic examination and were seen in clinic at 3-month intervals.

When required, it is possible to remove the stent. Because of its shape and ability to expand after implantation the Gianturco stent cannot be removed intact: it must first be fractured through the bronchoscope. This can be achieved by laser or mechanically, using an appropriate endoscopic instrument. The cut end of the wire is then grasped with biopsy forceps; by rotating the forceps the stent is made to unravel and rolled over the forceps, allowing its extraction through the bronchoscope.

Results

Placement was relatively straightforward and there were no immediate complications directly attributable to the insertion procedure. Mean operating time was 15 minutes, and all patients who were breathing spontaneously before the procedure were able to resume spontaneous respiration immediately afterward. Satisfactory stent positioning was achieved at the first attempt in 14 of 15 patients.

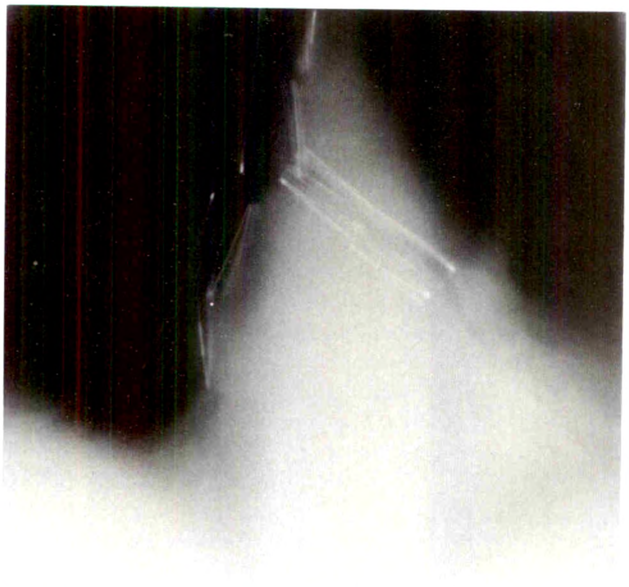


Fig 2. Plain chest radiograph showing three double-length stents in place in the trachea and both main bronchi.

An irritation-type cough and minor hemoptysis occurred in all patients. Coughing settled spontaneously in 10 patients within 5 days but required long-term inhaled steroid therapy in 5.

Follow-up endoscopy confirmed stable positioning with absence of displacement in all patients, with the stent becoming gradually covered by respiratory mucosa (Figs 3, 4). Sputum retention and secondary infection did not occur. Where a stent was placed across a bronchial orifice, usually in the right main bronchus across the upper lobe bronchial orifice, there was no interference with luminal patency.

Oblique frontal tomography also confirmed the absence of displacement, and plain chest radiography clearly demonstrated the gradual expansion in the diameter of the stent after placement (Fig 5). In patients with pure fibrous stenoses symptomatic improvement was good in 5 of 6 patients; the sixth has mild dysphagia. Minor granulomata appeared in 5 patients. These were all successfully photocoagulated with laser at follow-up endoscopy and resolved.

Three of 5 patients with tracheobronchial malacia had a good functional result: minor granulomata rapidly resolved with laser therapy in 2, the third requiring multiple endoscopy and photocoagulation. The fourth patient had a suction catheter entrapped within the stent necessitating stent removal. The fifth patient had a necrotic right bronchial wall with airway collapse at the time of stent placement; massive fatal hemoptysis developed due to erosion of the pulmonary artery 10 days after implantation.

Results were poor in the 4 patients with fibroinflammatory stenoses. There was severe granuloma formation, which was refractory to treatment with multiple endoscopy and laser therapy. Finally, the stents were removed with some difficulty in 3 patients, 2 of whom had subsequent silicone tube insertion with acceptable results.

Comment

No tracheobronchial prosthesis is entirely satisfactory. Where airway narrowing cannot be treated surgically the only therapeutic option may be to insert a stent. Most commonly used have been silicone tubes, which can be placed within the trachea or main bronchi with relative ease. They are well tolerated and can be effective in malignant disease as they help prevent luminal occlusion by endobronchial tumor [7]. Their main disadvantages are that they are liable to displacement and they obstruct any bronchial orifices that they cross. In addition, they interfere with normal mucociliary clearance of secretion; this may lead to build-up of mucus and secondary infection (both distal to the stent and between the stent and the airway wall) requiring frequent bronchial toilet and limiting their suitability for long-term use. It is primarily for these reasons that there has been recent interest in the

Table 1. Indications for Tracheobronchial Stent Placement

Type of Lesion	Patient No.	Cause	Position	No. of Stents
Pure fibrous stenosis	1	Postintubation for respiratory failure	Trachea	1
	2	Postintubation for respiratory failure	Trachea	3
	3	Postintubation for respiratory failure	Trachea	2
	4	Double-lung transplant	Right main bronchus	3
	5	Single-lung transplant	Right main bronchus	1
	6	Single-lung transplant	Right main bronchus	1
Fibroinflammatory stenosis	7	Postintubation, multiple previous interventions	Laryngotracheal	1
	8	Postintubation, multiple previous interventions	Laryngotracheal	1
	9	Postintubation	Trachea	1
	10	Papillomata	Laryngotracheal	1
Tracheobronchial malacia	11	Chronic respiratory insufficiency	Trachea	4
	12	Chronic respiratory insufficiency	Trachea & both main bronchi	4
	13	Chronic respiratory insufficiency	Trachea & left main bronchus	2
	14	Amyloidosis	Trachea & both main bronchi	3
	15	Double-lung transplant bronchial necrosis	Right main bronchus	1

use, albeit sporadic, of expanding wire stents in the tracheobronchial tree [8–10].

We had no difficulty in implantation. The endoscopic equipment required is standard and available in all thoracic surgical units. We used the rigid bronchoscope for implantation, but it is also possible to use a fiberoptic bronchoscope (with the introducer sheath alongside it) or to insert the stent under image intensifier control using previously placed radiopaque skin markers as locators and to confirm satisfactory positioning and function endoscopically at a later date. The latter technique is particularly useful in small children, in whom the airway may not be of sufficient caliber to allow full instrumentation.

Choice of length and, more importantly, diameter of the stent are crucial: too small a stent may be liable to displacement, and one that is too large may lead to

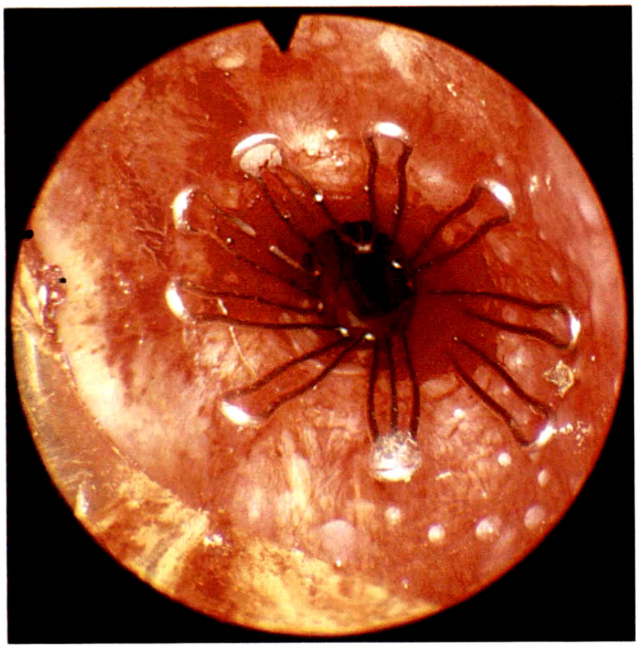


Fig 3. Endoscopic view of a stent in place at the time of insertion.

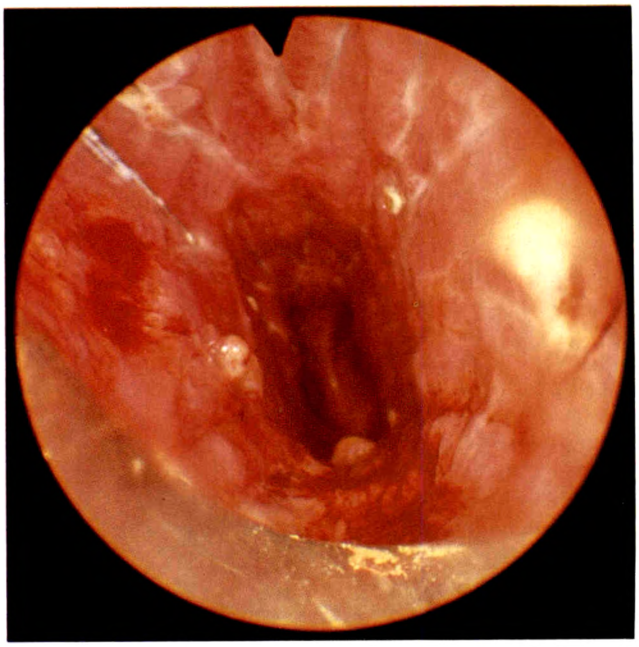


Fig 4. Same stent as in Figure 3 three months after implantation. The respiratory mucosa has partially covered the wire.

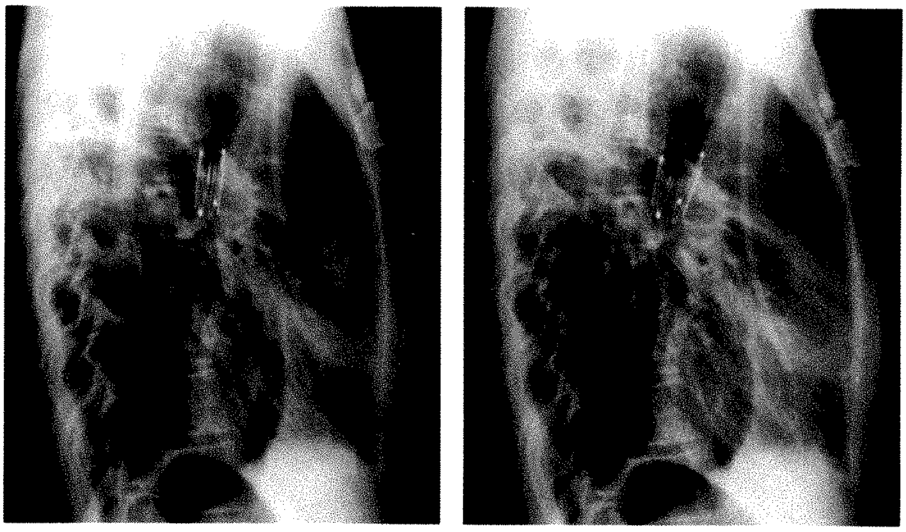


Fig 5. Gradual increase in the functional diameter of the stent: two radiographs taken a month apart.

esophageal compression and dysphagia or may erode into the mediastinum and great vessel with catastrophic results.

Once implanted, the stent needs little specialized care. Routine endotracheal intubation is possible if required; in the case of recently inserted high tracheal stents intubation under fiberoptic control may be advisable to avoid hooking the tube on one of the metal barbs. More importantly, in the intubated patient with a stent in situ, extreme caution is required during "blind" airway aspiration to avoid suction catheter entrapment (as occurred in patient 13 in our series). Use of suction catheters without side ports may help avoid this complication.

The stent was well tolerated by our patients, and any persistent irritation cough was successfully dealt with using inhaled corticosteroid therapy. As would be expected from a wire-frame stent, retained secretions and infection are not a problem.

We observed one instance of dysphagia with normal esophagoscopic appearances and very slight esophageal indentation at the level of the stent on contrast esophagography. The patient in question has a psychiatric history, and the dysphagia may be partly functional.

Long-term results appear to depend on the etiological indications: results were satisfactory in pure fibrous stenoses and tracheobronchial malacia with the exception of the patient with bronchial wall necrosis who subsequently suffered fatal massive hemoptysis from erosion into the pulmonary artery. We now consider that a breach in the integrity of the airway wall should be a contraindication to stent implantation. Results were poor in patients with fibroinflammatory pathology: continued inflammation and proliferation of granulomata led to eventual stent removal in 3 of 4 patients. We now delay implantation until all signs of active inflammation have subsided and therefore consider any mucosal proliferative process, whether malignant or inflammatory, as a contraindication.

We succeeded in removing the stents in 4 patients without immediate unwanted sequelae. The removal technique is similar to that of rolling spaghetti on a fork, but much more difficult and at least equally messy. The procedure is therefore time-consuming and often hindered by the well-embedded barbs. Removal may have to be piecemeal, requiring several fractures of the stent. For these reasons it would be better, if at all possible, to avoid the requirement for removal by careful patient selection in the first place.

Wire stents can contribute to the palliation of symptoms of inoperable narrowed airways with an outcome that appears to depend on case selection and careful sizing and implantation. Stent use should be exercised with caution until longer follow-up is available.

Addendum

Since the preparation of the manuscript, we understand that the Gianturco prosthesis has been withdrawn by the manufacturers pending design modifications.

References

1. Wright KC, Wallace S, Charnsangavej C, Carrasco CH, Gianturco C. Percutaneous endovascular stents: an experimental evaluation. Radiology 1985;156:69–72.
2. Putnam JS, Uchida BT, Antonovic R, Rösch J. Superior vena cava syndrome associated with massive thrombosis: treatment with expandable wire stents. Radiology 1988;167:727–8.
3. Carasco CH, Wallace S, Charnsangavej C, et al. Expandable biliary endoprosthesis: an experimental study. AJR 1985;145:1279–81.
4. Fingland RB, Weisbrode SE, DeHoff WD. Clinical and pathologic effects of spiral and total ring prostheses applied to cervical and thoracic portions of the trachea of dogs. Am J Vet Res 1989;50:2168–75.
5. Wallace MJ, Charnsangavej C, Ogawa K, et al. Tracheobronchial tree: expandable metallic stents used in experimental and clinical applications. Radiology 1986;158:309–12.
6. Rauber K, Franke C, Rau WS. Self-expanding stainless steel endotracheal stents: an animal study. Cardiovasc Intervent Radiol 1989;12:274–6.
7. Insall RL, Morritt GN. Palliation of malignant tracheal strictures using silicone T tubes. Thorax 1991;46:168–71.
8. Mair EA, Parsons DS, Lally KP. Treatment of severe bronchomalacia with expanding endobronchial stents. Arch Otolaryngol Head Neck Surg 1990;116:1087–90.
9. Varela A, Maynar M, Irving D, et al. Use of Gianturco self-expandable stents in the tracheobronchial tree. Ann Thorac Surg 1990;49:806–9.
10. Simonds AK, Irving JD, Clarke SW, Dick R. Use of expandable metal stents in the treatment of bronchial obstruction. Thorax 1989;44:680–1.

Extrapleural Pneumonectomy in the Treatment of Malignant Pleural Mesothelioma

David J. Sugarbaker, MD, Steven J. Mentzer, MD, and Gary Strauss, MD

Divisions of Thoracic Surgery and Hematology/Oncology, Brigham and Women's Hospital, Boston, Massachusetts

A technique for extrapleural pneumonectomy in diffuse, malignant, pleural mesothelioma is described. The technique used in a protocol at Brigham and Women's Hospital has resulted in improved operative mortality figures and length of hospital stay. The right-sided procedure is presented followed by differences in technique required by the left-sided approach.

(Ann Thorac Surg 1992;54:941–6)

Extrapleural pneumonectomy has been used by thoracic surgeons in the treatment of tuberculous empyema [1–3] as well as other pleural diseases such as malignant pleural mesothelioma [4–16]. Initial series reporting the efficacy of this procedure in mesothelioma were colored by its relatively high reported operative mortality [5, 6] when compared with standard pneumonectomy [17].

Over the last 8 years we have gained substantial experience in our institution with a procedure in the treatment of diffuse malignant pleural mesothelioma in a protocol using pleural pneumonectomy, cyclophosphamide, doxorubicin, and cisplatin (CAP) chemotherapy, and radiotherapy. Our surgical technique has evolved, and our operative mortality and length of hospital stay have continued to decrease.

We present a detailed account of our current technique of pleural pneumonectomy resecting lung, parietal and visceral pleura, pericardium, and diaphragm. Our technique differs from previous descriptions of the procedure [9, 18]. The technique for pleural mesothelioma varies depending on whether the procedure is performed on the right or the left side. We describe the surgical approach to the right side. After this, a brief description of the unique aspects of a left-sided approach will be discussed.

Material and Methods

Patient Selection

Patients selected for extrapleural pneumonectomy are those who have been enrolled in a protocol in which this technique is used as a means of control of the primary tumor. Resection is attempted only in Butchart clinical stage I and II patients. Primary resection is then followed by CAP chemotherapy and radiotherapy. Other adjuvant chemotherapy protocols are currently in development in both the United States and Europe [19, 20].

Selection of patients for the procedure is based on the usual parameters for defining operability in pneumonectomy patients. The use of forced expiratory volume in 1 second, as well as other dynamic spirometry testing in addition to functional oximetry, is helpful in defining these patients. In borderline recipients, the use of quantitative ventilation perfusion scanning may be of substantial benefit in predicting postoperative pulmonary function.

We use preoperative echocardiography to define ventricular function in this group of patients who are destined to receive doxorubicin as an adjuvant therapy. We have found the echocardiogram helpful in determining which patients will be able to sustain, not only the pneumonectomy, but also these postoperative adjuvant treatments. This baseline echocardiogram is used midway through the course of postoperative chemotherapy to further detect possible cardiac toxicity.

Preoperative chest magnetic resonance imaging has proved of substantial benefit in helping us determine extent of disease preoperatively, particularly the sagittal planes demonstrating evidence of disease in the paravertebral sulcus or disease extending through the diaphragm. In addition sagittal cuts are of help in predicting mediastinal involvement of the cava, esophagus, or trachea. The presence of any one of these findings precludes any attempt at operative resection.

In the cases where transdiaphragmatic involvement is suspected but not proven, a limited laparotomy is performed so that the surgeon may perform an inspection of the liver to determine the presence or absence of actual invasion.

We have found the use of routine preoperative echocardiography and magnetic resonance imaging extremely helpful in decreasing the number of patients in whom operative resection is precluded at the time of surgical exploration.

Clean surgical margins have not been shown to be of any benefit in predicting survivors in this disease [16], although every attempt is made for as complete a cytoreductive procedure as possible.

Technique

RIGHT-SIDED LESION. The incision for right-sided pleuropneumonectomy is an extended right thoracotomy along the course of the sixth rib (Fig 1). The incision is carried from the posterior aspect of the thorax, midway between the posterior scapular ridge and the spine, along the bed

---

Accepted for publication March 19, 1992.

Address reprint requests to Dr Sugarbaker, Division of Thoracic Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

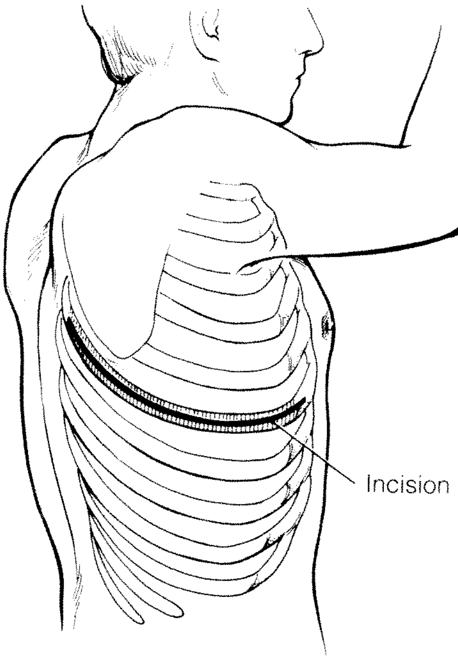


Fig 1. Extended right thoracotomy incision.

of the sixth rib to the costochondral junction. A subperiosteal resection of the sixth rib is then performed to provide wider exposure and to readily facilitate entrance into the extrapleural plane.

The periosteum is opened and a broad-based dissection is then begun superiorly toward the apex using blunt and sharp techniques. The dissection is completed along the anterior lateral aspect superiorly and then begun in a similar fashion inferiorly and laterally to the diaphragm. Care is taken to avoid dissection posterior to the azygos vein until wider exposure has been gained.

At this time two chest retractors are placed anteriorly and posteriorly. Continued blunt and sharp dissection occurs up to the cupola of the lung. Care is taken to palpate the course of the subclavian artery and to maintain the plane between the parietal pleural and these vessels.

Care is then taken to preserve the internal mammary artery and vein, which often pass through the extrapleural plane superomedially. If mistaken for adhesions, these can be avulsed from either the superior vena cava or the subclavian artery. Small adhesions are divided, staying close to the pleural plane in the extrapleural fat.

The dissection is then carried immediately from the apex of the lung to the azygos vein. Dissection is carried extrapleurally until the right upper lobe and main bronchus are clearly identified (Fig 2). The cava and azygos vein are then dissected with sharp as well as blunt dissection from the parietal pleural structures. Care is taken to prevent avulsion of the vein. The dissection is then continued anteriorly and inferiorly to the circumferential diaphragmatic margin.

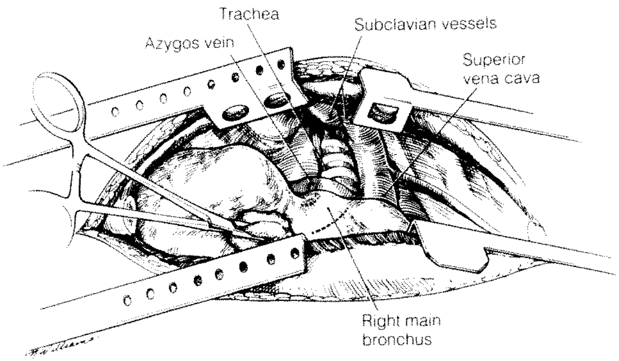


Fig 2. Right main bronchus identified.

A nasogastric tube is placed and facilitates palpation of the esophagus to preserve it from damage. The diaphragm is opened posterolaterally in a radial fashion to the anterior medial aspect of the pericardium. Care is taken to keep the pleural envelope intact; in certain situations this requires dissection of the pleural envelope off the diaphragm before its division (Fig 3).

Care is taken when dividing the diaphragm to preserve the underlying peritoneum. Blunt dissection is then used to wipe the peritoneum off the diaphragm with the aid of a sponge stick (Fig 4). Once the diaphragm has been divided anterolaterally to the pericardium it is then divided along the caval and esophageal hiatuses. This may be facilitated by entering the pericardium to define the course of the inferior vena cava through the diaphragm. The diaphragm and pleural envelope are then divided just lateral to the inferior cava and esophagus (Fig 5). The diaphragmatic incision is then completed.

The pericardium is then formally opened anteromedially to the phrenic nerve and the hilar vessels (Fig 6). Care is taken to keep the parietal pleural envelope intact.

The main pulmonary artery is dissected free from the cava and underlying superior pulmonary vein (Fig 7). The

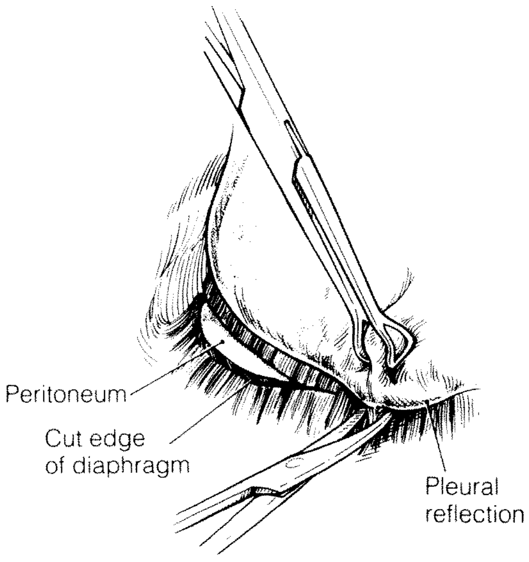


Fig 3. Dissection of the pleural envelope off the diaphragm.

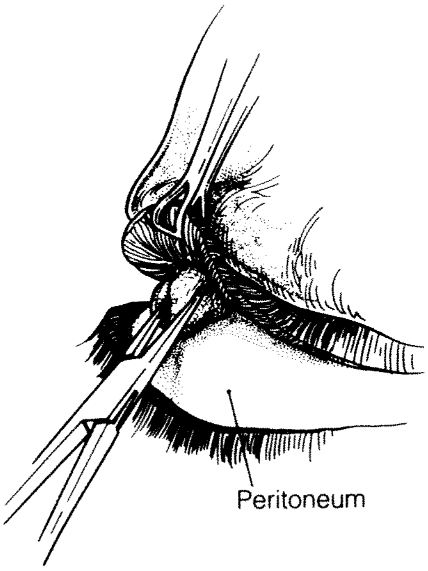


Fig 4. Peritoneum wiped off the diaphragm with a sponge.

intrapericardial right pulmonary artery is then divided between two vascular staple lines (see Fig 7) [21].

Once the pulmonary artery has been divided the superior pulmonary veins are likewise divided. The pericardium is divided posterior to the hilum to complete the pericardial resection. The specimen is then elevated and dissection continued posterior to the pericardium and lateral to the esophagus. A subcarinal node dissection is performed at this time. The main bronchus is then dissected to the carina and stapled using a heavy-gauge bronchial stapler (Fig 8). The specimen is removed.

A pericardial fat pad is then elevated (Fig 9) and placed over the bronchial stump. Then the pericardium is closed with a prosthetic patch using a monofilament suture (see Fig 9). The pericardium is always reconstructed on the right side to prevent cardiac herniation, a potentially fatal complication. Fenestrations are created in the patch to prevent tamponade.

Reconstruction of the diaphragm is then carried out. If peritoneal covering remains intact, multiple sutures of 0 Vicryl are used in a reefing fashion (Fig 10) to provide strength to the overlying peritoneum. The sutures are anchored in the chest wall (Figure 10). No further reconstruction is carried out.

If the peritoneum was not spared during dissection, a prosthetic impermeable patch is placed and sewn in place with a running monofilament 0 suture (Fig 11). We have

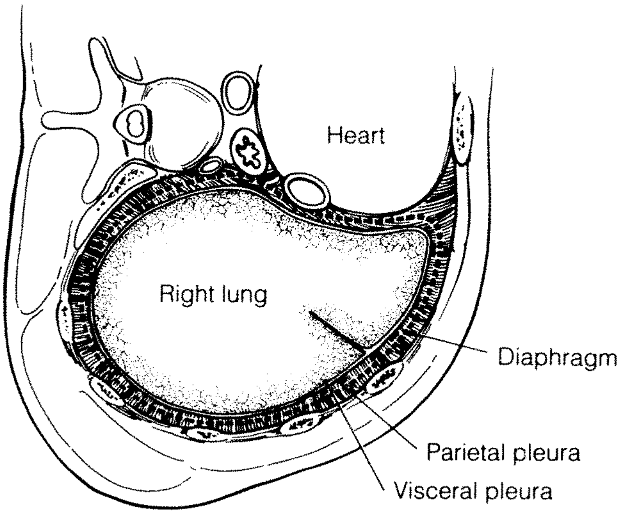


Fig 5. Diaphragm and pleural envelope divided lateral to inferior cava and esophagus.

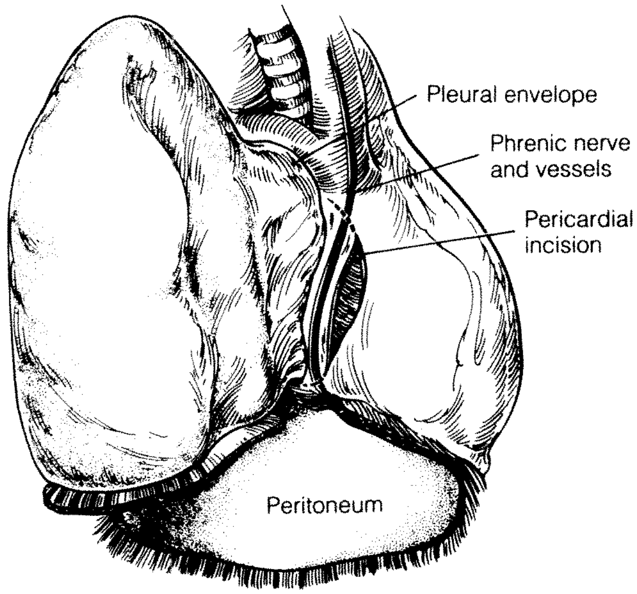


Fig 6. The pericardium is opened anteriorly medial to the phrenic nerve and hilar vessels.

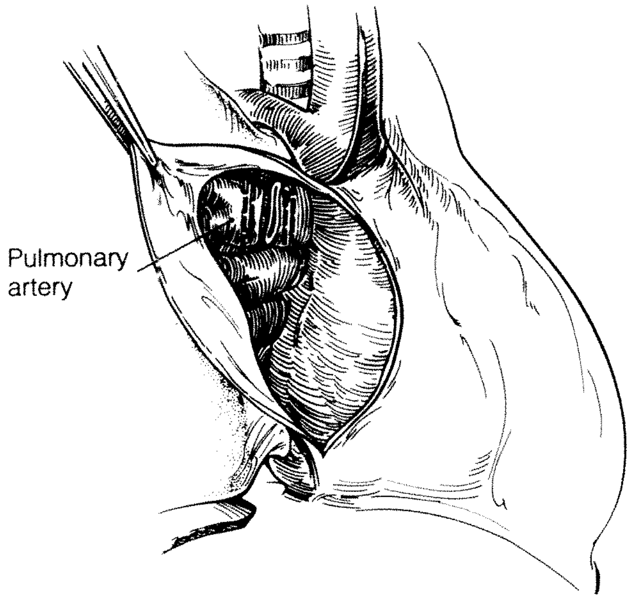


Fig 7. The intrapericardial right pulmonary artery is divided by two staple lines.

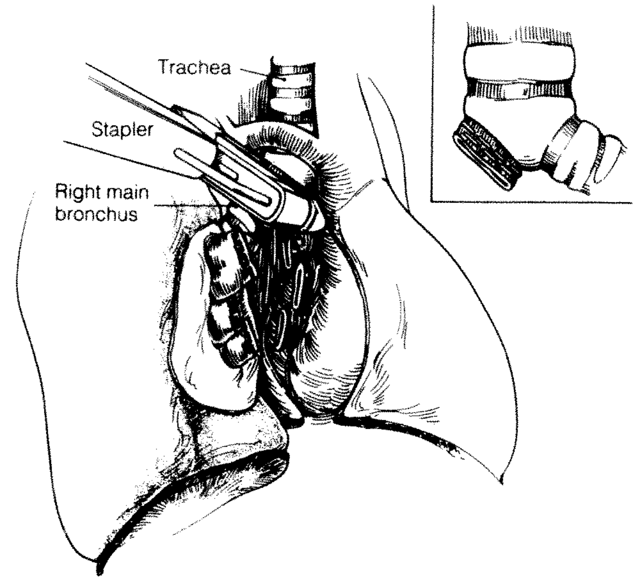


Fig 8. The main bronchus is dissected to the carina and stapled.

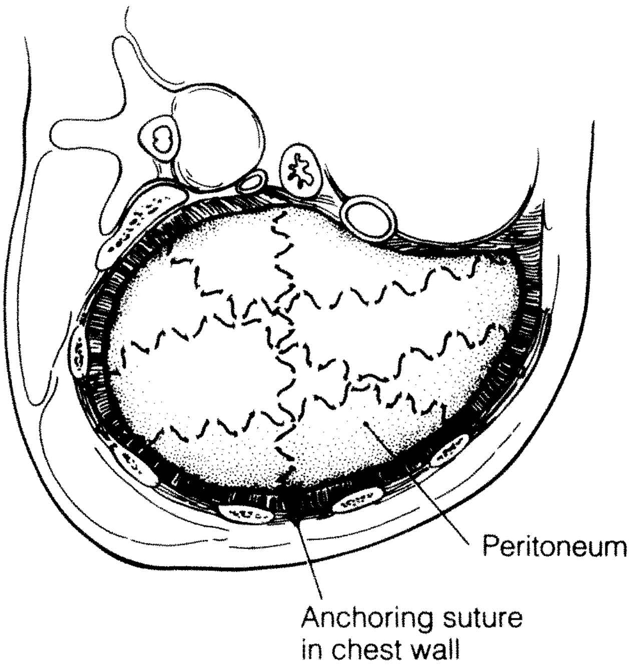


Fig 10. Reconstruction of the diaphragm using multiple sutures of 0 Vicryl in a reefing fashion is carried out; the sutures are anchored to the chest wall.

found the use of impermeable membranes prevents rapid filling of the chest cavity by peritoneal fluid. This rapid filling can produce mediastinal shift or tamponade in the early postoperative period before mediastinal stabilization has occurred.

The chest is then closed in multiple layers to assure watertight closure. A red rubber catheter remains until the skin is closed, and air (750 mL in women, 1,000 mL in men) is removed in the immediate postoperative period before leaving the operating room. A chest roentgenogram is obtained in the recovery room, and the catheter is removed if the mediastinum is midline. Air can be instilled or removed to balance the mediastinum if a shift is seen, and then the catheter is removed before the patient leaves the recovery room. Alternately, if oozing is present, a chest tube can be left to waterseal overnight.

Surgical specimens are assessed for resection margins in multiple areas. If gross disease, although limited, is left behind, it is outlined with clips for subsequent radiotherapy.

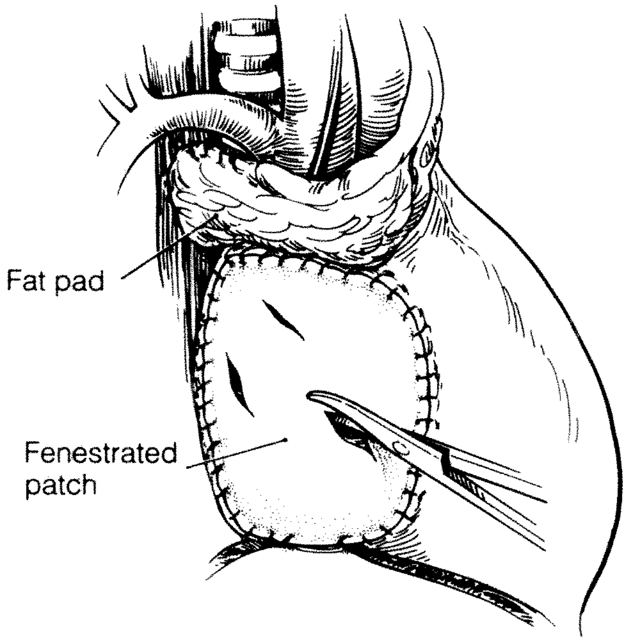


Fig 9. A pericardial fat pad has been sewn to cover the bronchial stump; the pericardium is closed with a patch, and fenestrations are made in the patch.

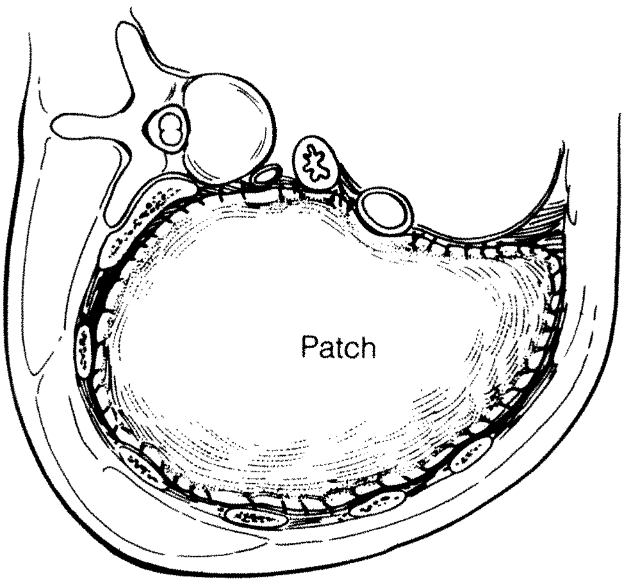


Fig 11. A prosthetic impermeable patch is sewn in place where the peritoneum has been removed.

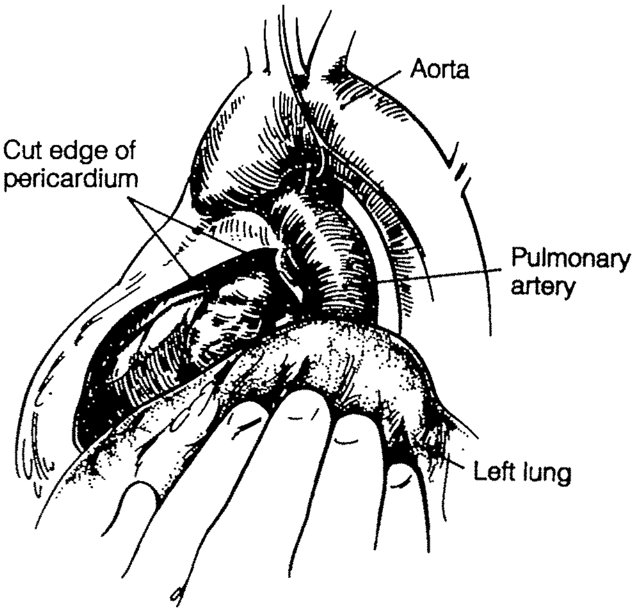


Fig 12. The pulmonary artery extrapericardial and extrapleural ready to be dissected.

LEFT-SIDED LESION. The approach for left-sided lesions is similar to that on the right. In our experience the procedure is technically easier on the left side due to the absence of the caval and esophageal hiatus. Subtle differences do exist. Less air needs to be removed from the left at the end of the procedure (500 mL in women; 750 mL in men).

In dissecting the medial aspect of the specimen in the posterior region, care must be taken to enter the correct plane in the preaortic region. One can get into an incorrect retroaortic plane and produce bleeding from avulsing the intercostal vessels. Care must be taken to assess tumor involvement of the aorta at this time.

Once the specimen has been circumferentially dissected from the chest wall, the diaphragm is divided in a radial fashion along the left side with care being taken to spare the aorta at the hiatus. The pericardium is then entered inferiorly and the vessels identified.

Unlike on the right side, we prefer to dissect the extrapleural left main pulmonary artery as it leaves the pericardium and enters the left chest. The pulmonary artery is divided in its extrapericardial, extrapleural position (Fig 12) using two vascular staple lines. The veins are taken from within the pericardium. The pericardial resection is then completed posteriorly.

The left main bronchus must be dissected for a greater distance to ensure a short bronchial stump. The bronchial stump is covered, the diaphragm reconstructed, and chest closed as on the right side. The pericardium is not routinely reconstructed on the left side because the risk of cardiac herniation is low on the left as opposed to the right.

HEMOSTASIS. Hemostasis during extrapleural pneumonectomy is a vital component to successful completion of this procedure. Aggressive use of the electrocautery is encouraged. In addition, rapid packing of areas after completion of dissection in that region is undertaken. After removal of the specimen, sheets of Surgicel (Johnson & Johnson, Arlington, TX) are placed over the raw chest wall surface. Packs are then placed on them and several minutes of tamponade is allowed to ensure a dry closure.

Clinical Results and Comment

The principles of this technique have been used in 44 consecutive cases of pleural pneumonectomy at the Brigham and Women's Hospital. Operative mortality was 4.6% (2 patients) and morbidity, 30% (13 patients). The mean length of stay was 10.2 ± 4.5 days for the 42 patients who survived operation.

The use of pleural pneumonectomy may be of increasing value in achieving cytoreduction in pleural malignant mesothelioma. As noted by others, the successful accomplishment of local control in this disease continues to exert substantial pressure for new and more effective chemotherapeutic adjuvant therapy [10].

It appears clear that in a disease where salvage rates of 15% to 20% over 5 years would represent a major advance, operative mortality rates must be held well below comparable levels if pleural pneumonectomy is to become a viable therapeutic alternative as a component of a multimodality approach to mesothelioma.

References

1. Hood RM, Antman K, Boyd A, Naidich D, Shemin R. Surgical diseases of the pleura and chest wall. Philadelphia: W. B. Saunders, 1986:126.
2. Sabiston DC Jr, Spencer FC. Surgery of the chest, 5th ed, vol I. Philadelphia: W. B. Saunders, 1990:705–6.
3. Sarot IA. Extrapleural pneumonectomy and pleurectomy in pulmonary tuberculosis. Thorax 1949;4:173–223.
4. Worn H. Moglichkeiten und Ergebnisse der chirurgischen Behandlung des malignen Pleuramesothelioms. Thoraxchir Vask Chir 1974;22:391–3.
5. Bamler KJ, Maassen W. The percentage of benign and malign pleura-tumors among the patients of a clinic of lung surgery with special consideration of the malign pleuramesothelioma and its radical treatment, including results of a diaphragm substitution of preserved dura mater. Thoraxchir Vask Chir 1974;22:386–91.
6. Butchart EG, Ashcroft T, Barnsley WC, Holden MP. Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. Thorax 1976;31:15–24.
7. DeLaria GA, Jensik R, Faber LP, Kittle CF. Surgical management of malignant mesothelioma. Ann Thorac Surg 1978;26:375–82.
8. Butchart EG, Ashcroft T, Barnsley WC, Holden MP. The role of surgery in diffuse malignant mesothelioma of the pleura. Semin Oncol 1981;8:321–8.
9. Faber LP. Malignant pleural mesothelioma: operative treatment by extrapleural pneumonectomy. In: Kittle CF, ed. Current controversies in thoracic surgery. Philadelphia: W. B. Saunders, 1986:80–4.
10. Antman KH, Shemin RJ, Corson JM. Malignant pleural mesothelioma: a combined modality approach. In: Kittle CF,

ed. Current controversies in thoracic surgery. Philadelphia: W. B. Saunders, 1986:68–75.
11. DaValle MJ, Faber LP, Kittle CF, Jensik RJ. Extrapleural pneumonectomy for diffuse, malignant mesothelioma. Ann Thorac Surg 1986;42:612–8.
12. Falkson G, Alberts AS, Falkson HC. Malignant pleural mesothelioma treatment: the current state of the art. Cancer Treat Rev 1988;15:231–42.
13. Dogan R, Cetin G, Moldibi B, et al. Traitement chirurgical du mesotheliome pleural. Rev Pneumol Clin 1988;44:57–63.
14. Landa L, Fianchini A, Gesuelli GC, Catalini GB, Fonti M. Il ruolo della chirurgia nel trattamento del mesotelioma pleurico. Chir Ital 1989;41:192–206.
15. Harvey JC, Fleischman EH, Kagan R, Streeter OE. Malignant pleural mesothelioma: a survival study. J Surg Oncol 1990; 45:40–2.
16. Sugarbaker DJ, Heher EC, Lee TH, et al. Extrapleural pneumonectomy, chemotherapy, and radiotherapy in the treatment of diffuse malignant pleural mesothelioma. J Thorac Cardiovasc Surg 1991;102:10–5.
17. Choi NC, Mathisen DJ, Huberman MS, Mark EJ. Cancer of the lung. In: Cancer manual, 8th ed. Boston: American Cancer Society, Massachusetts Division Inc, 1990:198.
18. Kittle CF. Pleural mesothelioma. In: Grillo HC, Austen WG, Wilkins EW Jr, Mathisen DJ, Vlahakes GJ, eds. Current therapy in cardiothoracic surgery. Toronto: B. C. Decker, 1989:114–6.
19. Boutin C, Viallat JR, Astoul P. Treatment of mesothelioma with interferon gamma and interleukin 2. Rev Pneumol Clin 1990;46:211–5.
20. Boutin C, Viallat JR, Van Zandwijk N, et al. Activity of intrapleural recombinant gamma-interferon in malignant mesothelioma. Cancer 1991;67:2033–7.
21. Sugarbaker DJ, Mentzer SJ. Improved technique for hilar vascular stapling. Ann Thorac Surg 1992;53:165–6.

Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hilton Executive Conference Center, Dallas Fort Worth Airport, Dallas, TX, on February 13, 1994. The closing date for registration is August 1, 1993.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Considerations in the Skeletonization Technique of Internal Thoracic Artery Dissection

James M. Cunningham, MD, Mohammad A. Gharavi, MD, Rostam Fardin, MD, and Raymond A. Meek, MD

California Center for Cardiothoracic Surgery, Thousand Oaks, California

Skeletonization of the internal thoracic artery during myocardial revascularization procedures may provide some degree of protection from sternal wound infection in diabetic, obese, or pulmonary compromised patients when both internal thoracic arteries are used as conduits. Prior descriptions of the technique fail to provide specific details and possible pitfalls of the dissection. A method of skeletonization that has been used at the California Center for Cardiothoracic Surgery in more than 1,000 patients is presented in detail. Potential advantages and disadvantages are discussed.

(Ann Thorac Surg 1992;54:947–51)

The excellent long-term results obtained in primary and secondary myocardial revascularization procedures that use the internal thoracic artery (ITA) as a conduit are well established [1–4]. Reports also indicate improved long-term survival rates if bilateral ITA grafts are placed [5]. However, the dissection of both ITA pedicles may be associated with an increase in sternal wound complications in obese, diabetic, or pulmonary compromised patients [6, 7].

One factor that may affect the sternotomy infection rate after bilateral ITA dissection is the ITA procurement technique [7, 8]. In patients receiving bilateral ITA grafts during primary coronary artery bypass procedures, Galbut and associates [9], using ITA skeletonization, reported a 1.5% incidence of postoperative sternal wound infection. In a smaller series of patients, Kouchoukos and co-workers [7], using ITA pedicles, noted a 6.9% sternal infection rate.

At the California Center for Cardiothoracic Surgery, skeletonization of the ITA is the dissection technique of choice for myocardial revascularization procedures. From November 1, 1988, to November 30, 1991, one or more ITAs have been used in 1,029 of 1,366 patients undergoing initial or redo coronary artery bypass procedures for a use rate of 75%. Sternotomy infection has occurred in 5 patients (0.5%). Although we cannot attribute the low infection rate to harvesting technique, our opinion is that the limited disruption of the periosteal arterial plexus, lymphatics, and soft tissue during the dissection does exert a positive influence on sternal healing.

Although the anatomy of the ITA as well as the specifics of ITA harvesting using a pedicle have been well described in standard texts and articles, little mention is made of skeletonization techniques [10–20]. Also, despite the basic description of ITA skeletonization provided by Galbut and associates [9], some cardiac surgeons who are quite familiar with the various pedicle techniques of ITA harvesting may not be comfortable with the prospect of skeletonizing the ITA. The purpose of this article is to provide the specific details, the potential advantages, and possible disadvantages of a skeletonization technique that has been used at the California Center for Cardiothoracic Surgery for the past several years. For those surgeons who may wish to consider skeletonization as an alternative technique, we hope to minimize the "learning curve" by providing the specifics as well as the inherent pitfalls of the dissection.

Operative Technique

In our opinion, a headlight and 2.5× or 3.5× magnifying loupes are helpful. A standard median sternotomy incision is used with only rare application of bone wax. Later dissection of the ITA is easier if meticulous hemostasis is obtained on the sternal edges to avoid aggravating accumulation of blood in the field. The thymic isthmus and prepericardial tissues are divided, but the pericardium is left intact.

Either a standard sternal retractor or a modified Favaloro retractor is used to elevate the left or right sternal half, and the table is rotated slightly away from the surgeon. The surgeon may either stand or sit as he or she prefers while doing the dissection.

The loose areolar tissue and pleural reflection immediately posterior to the sternum are dissected away using a *low* cautery setting (coagulation only, no cutting) and allowed to fall posteriorly. Often one or two branches of the ITA or tributaries of the internal thoracic vein (ITV) are encountered during this phase of the dissection as they leave the chest wall running posteromedially. These branches can be cauterized as they are well away from the ITA proper or controlled with fine tantalum Hemoclips (Edward Weck & Co, Research Triangle Park, NC) and divided. One of us (J.M.C.) prefers to use clips at this time to check for any flaws in the clip appliers. The tips of the

---

Accepted for publication March 24, 1992.

Address reprint requests to Dr Cunningham, Columbus Cardiothoracic and Vascular Surgical Associates, 2522 Warm Springs Rd, Columbus, GA 31904.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

appliers must meet exactly or the ITA branches can be torn during closure of the instrument. It is better to discover a defective instrument at this time than to possibly injure the ITA during later dissection.

Once the loose tissue is dissected away, one can usually see or palpate the ITA 3 to 4 cm from the sternal edge. Dissection may begin anywhere along the course of the artery but is usually begun at its midpoint and continued distally. The cautery tip is bent 45 to 60 degrees and an initial 4- to 5-cm cut is made in the endothoracic fascia well medial to the artery and vein. To avoid thermal injury to the ITA, it is extremely important to keep the cautery setting on low throughout the dissection. The edge of the endothoracic fascia is then grasped with a forceps (DeBakey or similar type) and, using the tip of the *cold* cautery as a dissector, the artery is better visualized and exposed. The artery can then be gently teased away from the chest wall, accompanying veins, fascia, lymphatics, and adipose tissue using the cautery tip. Forceps never touch the artery itself but may grasp the small remnants of soft tissue that continue to cling to the adventitia of the ITA. The initial cut in the endothoracic fascia is extended once the exact course of the ITA is determined. Inferiorly, fibers of the transversus thoracis muscle often must be divided to obtain adequate exposure.

Throughout the dissection, the ITA is intermittently sprayed with a dilute papaverine solution to minimize spasm and prevent desiccation. A relatively constant finding is a gradual increase in ITA diameter as proximal branches are divided and the vessel is freed of soft tissue and fascial constraints. Care is taken to keep well away from the ITA when using the cautery even in the "low" setting.

Dissection proceeds inferiorly until the terminal division of the ITA into its lateral musculophrenic and medial superior epigastric branches is well visualized. Terminal division usually occurs at the sixth intercostal space. These terminal branches are left intact to allow blood flow through the ITA until it is ready for use. Branches are divided between clips using a fine-pointed scissors or knife. Care is taken not to place the clip flush with the ITA for two reasons. First, if the clip is applied too close to the ITA, there is a chance the lumen will be narrowed or adventitia trapped in the clip may cause distortion of the natural lie of the vessel. Second, should the first clip either slip or cut through the branch, there is space for application of a second clip. Once branches are controlled, scissors or low cautery are used to divide remaining medial and lateral soft tissue attachments.

After the distal portion of the artery is freed, an additional cautery cut in the endothoracic fascia is made to allow dissection superiorly. Most branches will run anteriorly or laterally and are easily controlled. However, there are usually one or two branches that are directed anteromedially. These branches are sometimes hidden by adipose or lymphatic tissue, which can be quite adherent to the ITA. Meticulous technique is necessary to avoid tearing these branches or, worse, avulsing them from the ITA itself.

Should a tear or avulsion occur, small atraumatic vascular clamps are applied proximally and distally, thus allowing adequate visualization. Precise sutures of 8-0 polypropylene can then be placed without compromising the ITA lumen.

The proximal third of the ITA occasionally has large anterior perforating branches that may initially seem to be too short to allow satisfactory clip application. With careful dissection proximally and distally to the branch, suitable length can usually be obtained. One must not apply excessive traction on the ITA as these branches can tear easily, causing serious bleeding. If insufficient branch length precludes safe application of two clips, it is best to apply a clip to the ITA side of the branch. The branch is then cut and the cautery is used to obtain hemostasis on the chest wall.

Superiorly, the ITA follows the curve of the chest wall as it approaches its origin from the subclavian artery. In this area, dissection can be hampered and visualization obscured by lung ventilations. A strategically placed malleable retractor provides excellent exposure in this situation.

As the origin of the ITA is approached, pericardial branches are identified and divided. To obtain maximum ITA length, diameter, and flow, the highest chest wall branches must be visualized and securely divided. At this point of the dissection, it may be necessary to divide the ITV to obtain satisfactory exposure of these proximal branches. If the ITV lies anterior to the ITA, it may usually be left intact, whereas, if it crosses posterior to the ITA, it is usually divided. Frequently, a tributary enters the ITV at the point at which the ITV crosses posterior to the ITA. Although small, this tributary should be clipped or cauterized to avoid troublesome bleeding during the final stages of dissection.

While the retractor is still in place and exposure is good, the loose tissue connecting the superomedial pleural reflection to the chest wall is divided with cautery. This maneuver increases the usable length of the artery as it allows the ITA to drop into a "groove" when its distal end is divided later in the procedure. Most importantly, this maneuver also allows the ITA to lie intrapericardially as it courses to the selected coronary target vessel. Because the ITA now lies medial and posterior to the lung, ventilations do not produce any notable stretch or distortion of the ITA. Additionally, the artery is somewhat protected from injury should resternotomy be required. With this technique, pleural entry is usually avoided.

The vessel is then carefully inspected for any signs of inadequate hemostasis or wall trauma. Bleeding points are controlled with a clip or fine suture. It is not unusual to notice small areas of adventitial blood staining at clip application points. As previously mentioned, a clip will occasionally partially cut through a branch, causing bleeding and localized staining. It is extremely important to minimize adventitial blood staining by applying another clip if possible. When necessary, one can momentarily occlude the ITA to allow placement of a suture. In our experience, these small, well-localized areas of staining do not preclude use of the ITA. However, longer areas of wall hematoma or wall discoloration are worrisome as they can be associated with intimal tears and dissection. Should distal dissection be suspected, this portion of the ITA is discarded. Often, the ITA may still reach the intended target vessel without undue tension if the coronary lesions are sufficiently proximal. If the dissection or hematoma is proximal, the involved segment is removed and the ITA used as a free graft if possible. In our opinion, the ITA should not be used if a major wall hematoma or suspected dissection is identified along its midportion.

The artery is palpated to confirm the presence of a strong pulse. The ITA is left intact and wrapped in a papaverine-soaked sponge, and heparin is administered. The usual preparations for bypass are instituted. Should any doubt exist as to the quality of the ITA, distal division is carried out before bypass. Flow rate can then be measured directly and appropriate decisions made as to usability. Measured flow rates are usually greater than 150 mL/min. Flow rates less than 100 mL/min may increase substantially with gentle dilation. Should the flow rate remain less than 100 mL/min or if a strong pulse is not palpable, the ITA may, in some instances, still be used as a free graft. Obviously, systemic hypotension should be corrected and pressure on the subclavian artery or ITA caused by sternal elevation minimized as these factors can also contribute to decreased flow.

Comment

In our opinion, when using the ITA for myocardial revascularization, the surgeon's goal should be to secure a nontraumatized artery of maximum length and diameter with flow sufficient to provide adequate perfusion to selected areas of ischemic myocardium. This increase in perfusion may be accomplished using a single distal anastamosis or sequential grafts to two or more vessels. With careful dissection, good results can be obtained whether the ITA is procured as a pedicle, free graft, or a skeletonized vessel.

There is no doubt that the ITA graft obtained as a pedicle functions well in myocardial revascularization procedures [1–5, 12–15, 18]. Recently, Brown and Dougenis [21] reported satisfactory experience with a modified pedicle technique. The pedicle includes the ITA and ITV but the endothoracic fascia is removed, thus increasing ITA length. A retractor adaptor facilitates the dissection by providing improved exposure [21].

Despite these excellent results, the skeletonization procedure may have definite advantages. The diameter and usable length of the ITA are immediately known. Therefore, a decision as to its suitability for sequential grafting can be made early in the procedure. The quality of the vessel is easily ascertained by visual inspection and palpation of the pulse. "Borderline" arteries are readily identified and appropriate maneuvers instituted to remedy the problem if possible. In our experience, spasm is uncommon, but a 1.5- to 2.0-mm probe is occasionally used to allow *gentle* dilation if spasm is suspected. Because the ITA is free of surrounding veins, fascia, and lymphatic tissue, the natural lie of the artery is readily apparent and sequential anastomoses are technically easier to construct.

The chance of injury to surrounding structures is minimized with this technique. Skeletonization allows the phrenic nerve, venae comitantes, and lymphatic channels to remain undisturbed as the dissection progresses. The phrenic nerve descends on the anterior surface of the cupola of the pleura and enters the thoracic cavity between the subclavian artery and vein. It is here that phrenic nerve injury is most likely to occur during dissection because the nerve is intimately associated with the ITA as it crosses anterior or, most commonly, posterior to the vessel. With the skeletonization technique, surrounding tissue is gently pushed away from the ITA with the tip of the cold cautery. This method of dissection thus affords the nerve considerable protection from inadvertent injury.

Recently, O'Brien and others [22] have described significant impairment of phrenic nerve function and perfusion in an adult swine model if the pericardiacophrenic artery is divided during ITA harvesting. In our series, transient as well as permanent phrenic nerve paralysis has occurred but appears to be the result of direct cold trauma to the nerve from the use of intrapericardial iced slush. We doubt that devascularization of the phrenic nerve has contributed to this complication in our patients as no phrenic nerve paralysis has been observed since institution of the routine placement of an insulated pad during topical cooling.

The limited periarterial dissection and minimal use of cautery may aid in the preservation of collateral blood supply to the sternum [23, 24]. This factor is of minor importance in most patients but may significantly decrease the risk of sternal infection or delayed wound healing in diabetics who undergo unilateral or bilateral ITA grafting [8, 25]. We agree with Lehtola and associates [26], who recommend caution when using the cautery near the ITA. They report a clearly visible zone of endothelial damage occasionally associated with mural thrombus if the cautery contacts the ITA wall or a clip parallel to the wall. These injuries may remain undetected only to lead to possible graft occlusion later [26].

In our opinion, other possible advantages of the technique include minimal blood loss during dissection, few patient complaints of postoperative chest wall paresthesias, and infrequent pleural entry. Clipping of arterial branches, judicious use of the electrocautery, and little disruption of surrounding tissues minimize blood loss and may aid in limiting chest wall paresthesias. This technique allows the pleura to fall posterolaterally, thus affording some protection from inadvertent entry. As stated previously, skeletonization allows the ITA to lie entirely intrapericardially, medial and posterior to the lung; therefore, there is no need for routine pleural entry. Although small pleural effusions are commonly observed after this technique of ITA dissection, serious accumulations are seen infrequently.

Studies by Landymore and Chapman [27] have shown that the ITA is nourished primarily by luminal diffusion. Therefore, careful skeletonization should not exert any detrimental effects on ITA viability. The excellent long-term results reported using both free and skeletonized ITA grafts support this assumption [9, 28].

The skeletonization technique does have potential disadvantages, however. The time required for dissection is increased when compared with the pedicle technique. Currently, our average dissection time is approximately 20 to 25 minutes, whereas prior experience has shown an ITA pedicle can be freed in 10 to 15 minutes. The extra time and effort expended in skeletonization have had no adverse effect on perioperative morbidity or mortality in our series. We have also used the technique during emergency procedures after failed percutaneous angioplasty in suitable patients.

There is an increased risk of ITA injury resulting in dissection or a serious wall hematoma if meticulous technique is not observed. With experience, patience, and scrupulous attention to detail, intraoperative trauma to the ITA is infrequent. In our series, less than 1% of ITAs have been considered unsuitable for use because of dissection trauma, small size, or inadequate flow characteristics.

In conclusion, this technique of ITA skeletonization has consistently produced a satisfactory conduit for myocardial revascularization procedures performed in more than 1,000 patients at the California Center for Cardiothoracic Surgery. We have adopted ITA skeletonization not only because of the vessel length, diameter, and flow obtained but also because of the limited perivascular tissue disruption that occurs during the dissection. Although we believe that it is the technique of choice for the reasons listed above, it may be especially useful in diabetic, obese, or pulmonary compromised patients if bilateral ITA harvesting is being considered.

References

1. Grondin CM, Campeau L, Lesperance J, Enjalbert M, Bourassa MG. Comparison of late changes in internal mammary and saphenous vein grafts in two consecutive series of patients 10 years after operation. Circulation 1984;70(Suppl 1):208–12.
2. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. N Engl J Med 1986;314:1–6.
3. Sing RN, Sosa JA, Green GE. Long-term fate of the internal mammary artery and saphenous vein grafts. J Thorac Cardiovasc Surg 1983;86:359–63.
4. Cameron A, Kemp HG, Green GE. Bypass surgery with internal mammary artery graft: 15 year follow-up. Circulation 1986;74(Suppl 3):30–6.
5. Fiore AC, Naunheim KS, Dean P, et al. Results of internal thoracic artery grafting over 15 years: single versus double grafts. Ann Thorac Surg 1990;49:202–9.
6. Culliford AT, Cunningham JN Jr, Zeff RH, Isom OW, Teiko P, Spencer FC. Sternal and costochondral infections following open-heart surgery: a review of 2594 cases. J Thorac Cardiovasc Surg 1976;72:714–26.
7. Kouchoukos NT, Wareing TH, Murphy SF, Pelate C, Marshall WG. Risks of bilateral internal mammary artery bypass grafting. Ann Thorac Surg 1990;49:210–9.
8. Grossi EA, Esposito R, Harris LJ, et al. Sternal wound infections and use of internal mammary artery grafts. J Thorac Cardiovasc Surg 1991;102:342–7.
9. Galbut DL, Traad EA, Dorman MJ, et al. Seventeen-year experience with bilateral internal mammary artery grafts. Ann Thorac Surg 1990;49:195–201.
10. Kubik S, Healey JE. Surgical anatomy of the thorax. Authorized English ed. Philadelphia: Saunders, 1970:40–4.
11. Woodburne RT. Essentials of human anatomy. 3rd ed. New York: Oxford University Press, 1965:339–40.
12. Loop FD, Effler DB, Spampinato N, et al. Myocardial revascularization by internal mammary artery grafts. A technique without optical assistance. J Thorac Cardiovasc Surg 1972;63:674–80.
13. Green GE, Sosa JA, Cameron A. Prospective study of the feasibility of routine use of multiple internal mammary artery anastomoses. J Cardiovasc Surg (Torino) 1989;30:643–7.
14. Dion RA, Verhelst R, Goenen M, et al. Sequential mammary artery grafts in one hundred and twenty consecutive patients: indications, operative technique, 6 months post operative functional and angiographic controls. J Cardiovasc Surg (Torino) 1989;30:635–42.
15. Kabbani SS, Hanna ES, Bashour TT, et al. Sequential internal mammary-coronary artery bypass. J Thorac Cardiovasc Surg 1983;86:703–5.
16. Ochsner JL, Mills NL. Coronary artery surgery. 1st ed. Philadelphia: Lea & Febiger, 1978:164–72.
17. Stiles QR, Tucker BL, Lindesmith GG, Meyer BW. Myocardial revascularization: a surgical atlas. 1st ed. Boston: Little, Brown, 1976:122–9.
18. Geha AS, Baue AE. Early and late results of coronary revascularization with saphenous vein and internal mammary artery grafts. Am J Surg 1979;137:456.
19. Kirklin JW, Barratt-Boyes BG. Cardiac surgery. 1st ed. New York: Wiley, 1986:222–3.
20. Sabiston DC, Spencer FC. Surgery of the chest. 5th ed. Philadelphia: Saunders, 1990:1710–1.
21. Brown AH, Dougenis D. Dissection of the two internal mammary arteries with maximal exposure and minimal adverse sequelae by means of an inexpensive, simple, atraumatic retractor. J Thorac Cardiovasc Surg 1991;102:753–6.
22. O'Brien JW, Johnson SH, VanSteyn SJ, et al. Effects of internal mammary dissection on phrenic nerve perfusion and function. Ann Thorac Surg 1991;52:182–8.
23. Arnold M. The surgical anatomy of sternal blood supply. J Thorac Cardiovasc Surg 1972;64:596–610.
24. Seyfer AE, Shriver CD, Miller TR, Graeber GM. Sternal blood flow after median sternotomy and mobilization of the internal mammary arteries. Surgery 1988;104:899–904.
25. Hazelrigg SR, Wellons HA, Schneider JA, Kolm P. Wound complications after median sternotomy. J Thorac Cardiovasc Surg 1989;98:1096–9.
26. Lehtola A, Verkkala K, Jarvinen A. Is electrocautery safe for internal mammary artery mobilization? Thorac Cardiovasc Surg 1989;37:55–7.
27. Landymore RW, Chapman DM. Anatomical studies to support the expanded use of the internal mammary artery graft for myocardial revascularization. Ann Thorac Surg 1987;44:4–6.
28. Barner HB, Standeven JW, Reese J. Twelve-year experience with internal mammary artery for coronary artery bypass. J Thorac Cardiovasc Surg 1985;90:668–75.

INVITED COMMENTARY: Skeletonization of the ITAs: A Step Backward?

Historically, when the ITA was first used, Vineberg reported its use as a skeletonized vessel. Sewell popularized use of the ITA as a pedicle because of the ease and speed as well as the safety of takedown. This report advocates skeletonization of the internal thoracic artery with the hope that sternal wound problems would decrease as compared with patients in whom ITAs are taken down as pedicle grafts. Indeed, when one compares two reports of bilateral ITAs in the August 1990 issue of *The Annals of Thoracic Surgery*, the group with skeletonized ITAs fared better in relation to the incidence of sternal wound problems (1.5% in 1,087 patients compared with 6.9% in 246 patients). The number of diabetic patients was 22.6% and 23%, respectively. A third article in the same issue mentioned a 3% mortality secondary to sepsis, but mediastinal infection was not listed in their cohort, which included only 4% diabetic patients. Current data on bilateral ITAs harvested by skeletonization in 731 patients were presented at the Western Thoracic Surgical Association meeting in Kauai, Hawaii, June 24–27, 1992. In a 23% diabetic population a 1.4% incidence (10 patients) of sternal infection (7 diabetics, 3 nondiabetics) was found. There was no statistical difference when compared with 736 single ITA grafts (1.2%).

Other factors may come into play regarding sternal wound problems. There are differences among surgical groups in methods of sternal closure, use of bone wax, and antibiotic administration. I have noted that residents in training use the electrocautery on the sternum much more liberally to avoid having a patient undergo reexploration for bleeding. Cunningham and associates note in this report their electrocautery was used on the "low setting" with coagulation only and no cutting element. Because no numbers are given, I can only assume that the "low setting" is 20 to 30 W-s. Experience has shown that an electrosurgery instrument with a crest factor (voltage peak divided by voltage root mean squared) of 10 to 11 offers the least chance of thermal injury. Cunningham and associates list advantages of skeletonizing the ITA and, indeed, it seems logical that less cautery, less dissection, and less interruption of blood supply and lymphatics would result in fewer sternal wound problems.

Besides the penalty of a learning curve for ITA injury from harvest by skeletonization, one must question is there is a "late" penalty to be expected? We are all aware of the difficulties in obtaining postoperative angiograms; however, certainly since the initiation of these studies some of the patients who had skeletonization of the ITAs must have been restudied. It is imperative that Cunningham and associates present those data to confirm "late" safety of the procedure. Our early comparision [1] of pedicle versus skeleonized ITAs showed no intermediate ill effect of ITA skeletonization. It should be emphasized there is an increased hazard for an inadvertent twist of a skeletonized ITA, especially when routing the graft to areas other than the left anterior descending coronary artery. The usual anatomical features for orientation of such grafts are absent after skeletonization. Is routine use of the skeletonized ITA at this point a step backward? This we do not know. However, its use seems prudent in diabetic, obese patients when both ITAs are needed.

Noel L. Mills, MD

The Cardiology Center
4500 Wichers Dr (Marrero)
New Orleans, LA 70072

Reference

1. Mills NL, Ochsner JL. Technique of internal mammary-to-coronary artery bypass. Ann Thorac Surg 1974;17:237–46.

The Meadox-Gabbay Pericardial Xenograft: Failure of the Unicusp Principle

Uberto Bortolotti, MD, Paolo Ius, MD, Gaetano Thiene, MD, Marco Minarini, BS, Aldo Milano, MD, Carlo Valfrè, MD, Enrico Talenti, MD, Marialuisa Valente, MD, and Alessandro Mazzucco, MD

Departments of Cardiovascular Surgery, Pathology, and Radiology, University of Padova Medical School, Padova; and Department of Cardiovascular Surgery, Treviso Regional Hospital, Treviso, Italy

Durability of a new bioprosthesis, the Meadox-Gabbay unileaflet pericardial xenograft, was evaluated by reviewing a series of 12 patients who received this device in the mitral position from 1983 to 1985. Bioprosthetic failure necessitated reoperation in 5 patients 21, 22, 53, 66, and 81 months after placement. Three patients died of cardiac failure after 31, 52, and 70 months; no postmortem examinations were done. In 2 of the 3 patients, an echocardiographic study had shown signs of valvular dysfunction. Pathological examination of five available explants revealed the presence of redundancy and stretching of the single pericardial leaflet in all of them; in one, this lesion alone caused severe prosthetic incompetence. Other pathological findings included cusp and commissural calcification and commissural tears with or without calcification. Histologic examination and electron microscopy showed intrinsic calcification involving both collagen bundles and cellular debris and various degrees of collagen disruption. In this limited series of patients, the Meadox-Gabbay pericardial xenograft demonstrated various modes of failure that markedly impair its durability and render it unsuitable as a cardiac valve substitute.

(Ann Thorac Surg 1992;54:952–8)

The Meadox-Gabbay pericardial xenograft (Meadox Medicals, Inc, Oakland, NJ) is a bioprosthesis made of a single leaflet of glutaraldehyde-treated bovine pericardium mounted on a flexible Delrin stent [1]. Clinical use of this device was started in October 1983, and the preliminary results obtained in a multicenter study were considered satisfactory [2]. However, evaluation of this device in an experimental animal model showed that the durability of this bioprosthesis may be limited by multiple modes of structural deterioration [3]. Our experience seems to confirm these findings in the clinical setting.

Material and Methods

From November 1983 to February 1985, 12 patients underwent isolated mitral valve replacement with a Meadox-Gabbay unicusp pericardial xenograft (Table 1). There were 9 women and 3 men with a mean age of 56 years (range, 43 to 65 years). Ten patients had pure or predominant mitral stenosis, 1 had pure mitral regurgitation, and 1 had failure of a porcine mitral bioprosthesis. An associated surgical procedure was performed in 1 patient for excision of a left atrial myxoma. Preoperatively, all patients were in New York Heart Association functional class III or IV. One patient was in chronic renal failure requiring hemodialysis (patient 12); the indication to implant a tissue valve in this patient was an absolute contraindication to anticoagulant treatment because of the presence of a gastric ulcer. Nine patients were in atrial fibrillation and 3, sinus rhythm.

Surgical techniques were those usually employed for insertion of bioprosthetic valves at our institution [4]. All operations were performed with moderately hypothermic cardiopulmonary bypass, cold crystalloid cardioplegia, and topical cooling. All prostheses were implanted using single sutures buttressed by Teflon felt. The following prosthetic valve sizes were employed: 27 mm (4 patients), 29 mm (4 patients), and 31 mm (4 patients). Postoperatively, 6 patients were anticoagulated with warfarin sodium for an indefinite period, 5 were anticoagulated for a few months, and 1 was not anticoagulated; 1 patient was given antiplatelet drugs after suspension of oral anticoagulants.

Results

Clinical Data

There were no hospital deaths. During follow-up, 3 patients died with signs of cardiac failure 31, 52, and 70 months after mitral valve replacement. The cause of death was considered to be cardiac failure in all 3, but none underwent postmortem examination. In 2 of them, an echocardiographic study performed shortly before death showed prosthetic mitral incompetence in 1 (patient 8) and bioprosthetic stenosis caused by cusp calcification in another (patient 12).

Five patients underwent successful reoperation for bioprosthetic failure (see Table 1). Reoperation was required because of bacterial endocarditis after 22 months in 1

Accepted for publication March 30, 1992.

Address reprint requests to Dr Bortolotti, Istituto di Chirurgia Cardiovascolare, Centro di Cardiochirurgia "V. Gallucci," Università di Padova, Via Giustiniani, 2, 35128 Padova, Italy.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

(patient 9) and because of structural valve deterioration in 4 after 21 (patient 4), 53 (patient 7), 66 (patient 1), and 81 months (patient 6). One patient sustained a peripheral embolism 6 months after the initial operation and recovered after embolectomy (patient 1), and 1 had a cerebral embolism after 79 months with permanent neurological deficit (patient 10); neither was anticoagulated.

Four patients are currently alive with the original prosthesis 76, 80, 84, and 85 months after mitral valve replacement. Two are in functional class I and 2, class II. In all of them, recent echocardiographic studies have ruled out signs of mitral xenograft dysfunction.

Table 1. Summary of Clinical and Surgical Data

Patient No.	Age (y)	Sex	Disease	Operation[a]	Follow-up	Interval (mo)	Postoperative Complications/Echocardiogram
1	60	F	MS + MI	MVR (29)	Reoperation	66	Peripheral embolism (6 mo)
2	48	F	MS	MVR (29)	Died, heart failure	52	. . .
3	52	F	MS	MVR (31)	Alive, NYHA class I	84	Normal bioprosthesis on 2-D echo
4	50	M	MI, LA myxoma	MVR (31), excision of myxoma	Reoperation	21	. . .
5	55	F	MS	MVR (27)	Alive, NYHA class II	85	Normal bioprosthesis on 2-D echo
6	56	F	MS	MVR (31)	Reoperation	81	. . .
7	62	M	MS	MVR (29)	Reoperation	53	. . .
8	62	F	MS	MVR (29)	Died, heart failure	70	Bioprosthetic incompetence on 2-D echo
9	59	M	Failure of PMB	MBR (31)	Reoperation	22	Endocarditis
10	65	F	MS	MVR (27)	Alive, NYHA class II	80	Cerebral embolism (79 mo)
11	58	F	MS	MVR (27)	Alive, NYHA class I	76	Normal bioprosthesis on 2-D echo
12[b]	43	F	MS	MVR (27)	Died, heart failure	31	Calcific bioprosthetic stenosis on 2-D echo

[a] Size of Meadox bioprosthesis is given in millimeters in parentheses. [b] This patient was in chronic renal failure and required hemodialysis.

LA = left atrial; MBR = mitral bioprosthetic replacement; MI = mitral incompetence; MS = mitral stenosis; MVR = mitral valve replacement; NYHA = New York Heart Association; PMB = porcine mitral bioprosthesis; 2-D = two-dimensional.

Table 2. Pathological Findings in the Five Meadox-Gabbay Explants

Patient No.	Type of Dysfunction	Gross Findings	Ca^{2+} on Micro-radiography[a]	Histologic and Electron Microscopic Findings
1	Stenosis	Dystrophic calcification, cusp redundancy, commissural tear	+ + +	Collagen disruption, intrinsic and extrinsic calcification
4	Incompetence	Cusp redundancy	0	Collagen disruption, focal inflammatory infiltrates
6	Incompetence	Primary commissural tear	+[b]	Collagen disruption, focal inflammatory infiltrates
7	Stenosis	Dystrophic calcification, cusp redundancy, commissural tear	+ + +	Collagen disruption, intrinsic calcification, focal inflammatory infiltrates
9	Stenosis	Vegetative infective endocarditis, calcification, cusp redundancy	+ +	Collagen disruption, vegetations, gram-positive cocci, intrinsic and extrinsic calcification, focal inflammatory infiltrates

[a] Grading was as follows: 0 = absent; + = mild; + + = moderate; + + + = severe. [b] There was mild calcification on the pericardium covering the stent.

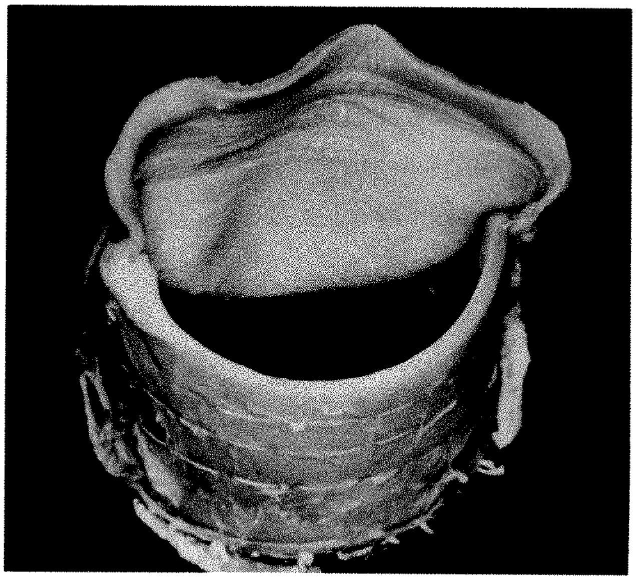


Fig 1. (Patient 4.) Gross view of a Meadox-Gabbay unicusp pericardial xenograft explanted 21 months after mitral valve replacement because of severe regurgitation. Note the redundancy of the single leaflet with infolding of the free margin. The commissures are intact.

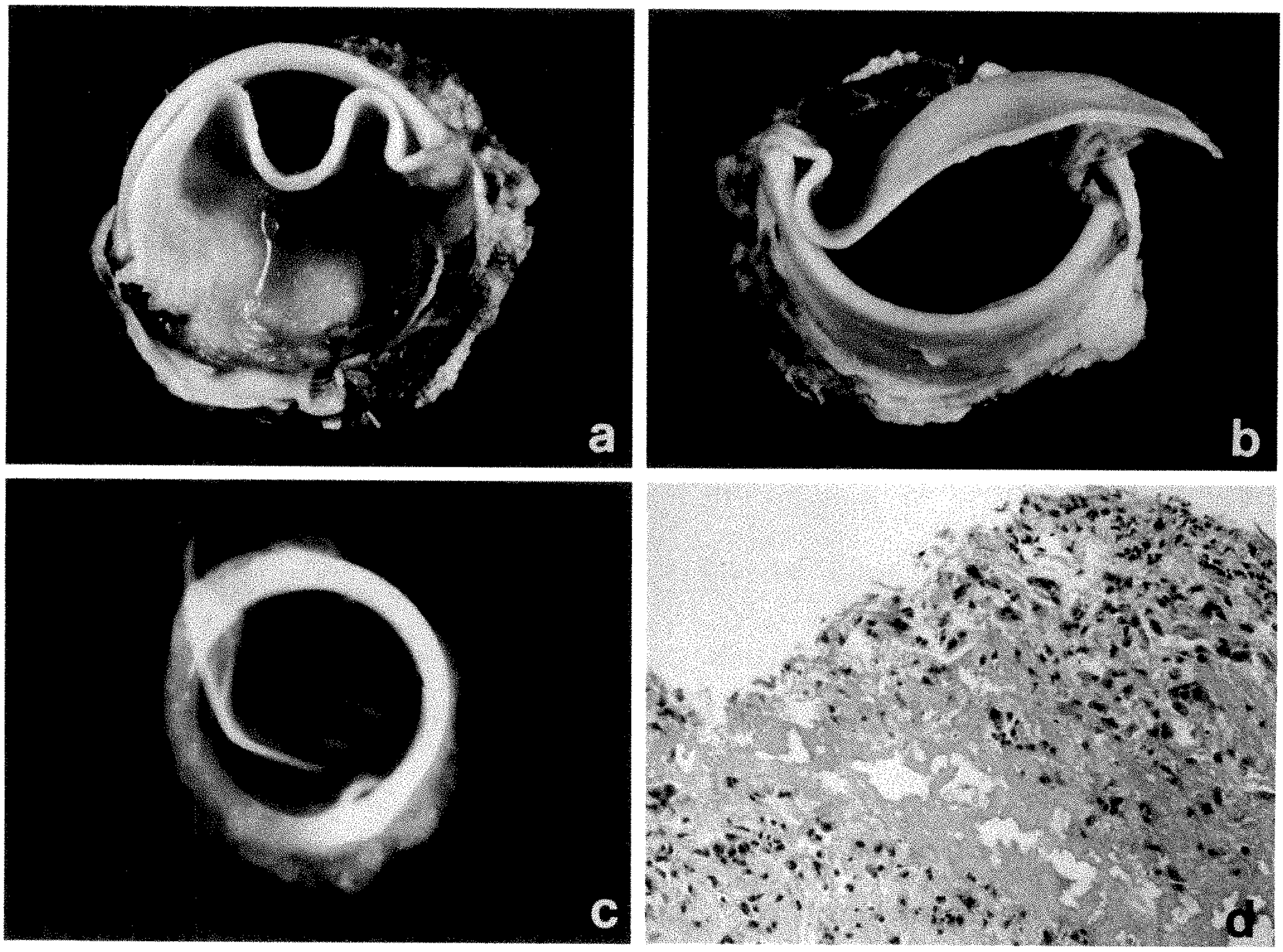


Fig 2. (Patient 6.) Pericardial xenograft removed after 81 months because of severe incompetence. Gross inspection showed (a) infolding of the cusp and (b) a deep commissural tear. (c) Microradiography disclosed that the tear was not related to calcification and that mild calcification was present on the pericardium covering the stent. (d) Inflammatory infiltrates and plasma insudation were observed within the cusp tissue close to the tear. (Hematoxylin and eosin; ×120 before 22% reduction.)

Pathological Data

Five Meadox-Gabbay bioprostheses were available for morphologic study (Table 2). Gross, histological, microradiographic, and ultrastructural examinations were done according to techniques previously reported by our group [5, 6]. At gross inspection, all explants exhibited some degree of cusp redundancy with infolding of the free margin. The type of dysfunction was incompetence in two and stenosis in three. Incompetence was caused by severe isolated cusp redundancy and stretching in one instance (Fig 1) and by cusp tears at the commissures without calcification in another (Fig 2). Stenosis was the consequence of massive primary dystrophic calcification in two explants (Fig 3), one of which showed an impending calcium-related commissural tear. The last xenograft showed vegetative infective endocarditis, found to be caused by gram-positive cocci, superimposed on primary dystrophic calcification (Fig 4). Mild calcification involving the pericardium covering the stent was observed in only one explant.

At histologic examination, calcifications were mainly intrinsic to the tissue. Focal inflammatory infiltrates were observed in all but one explant (see Fig 2d) and were particularly evident in the bioprosthesis with infective endocarditis. At electron microscopy, calcific deposits involved mainly collagen fibers and, more rarely, cellular debris (Fig 5). Various degrees of plasma protein insudation and collagen disruption were seen in areas close to cusp tearing.

Comment

Pericardial xenografts were introduced into clinical use by Ionescu and colleagues in 1970 [7], having the advantage of better hemodynamic characteristics compared with standard porcine bioprostheses [8]. First-generation pericardial bioprostheses were manufactured by individually sewing three separate leaflets of tissue to a supporting stent to replicate the anatomy of an aortic valve. However, leaflet abrasion against the fabric cloth covering the stent and the alignment stitches used to reinforce the commissures were subsequently recognized as major

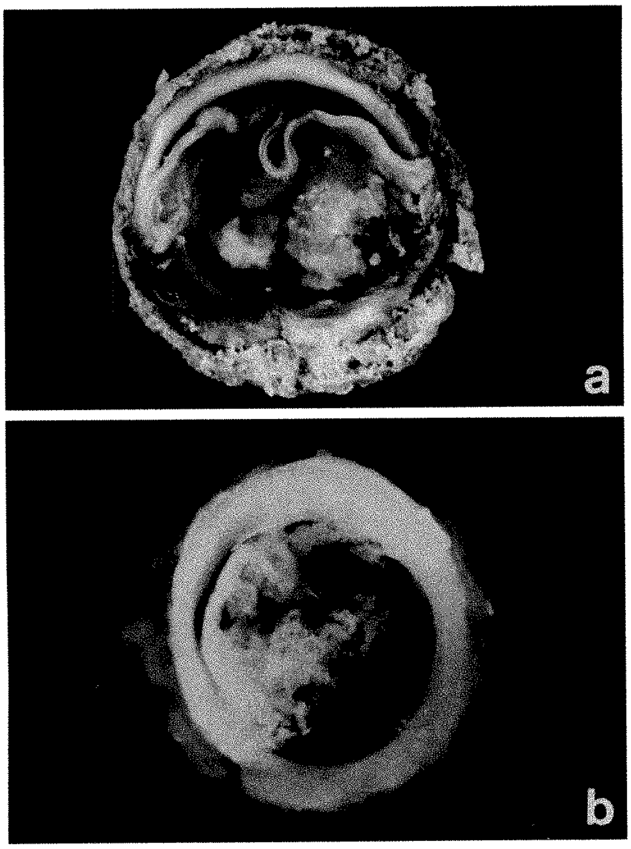


Fig 3. (Patient 1.) Pericardial xenograft explanted after 66 months because of stenosis. Massive dystrophic calcification was present at both (a) gross examination and (b) microradiographic examination.

weak points of such devices [9–13], as they were responsible for an unacceptably high rate of early failure mainly because of primary cusp tears [14–16]. These results clearly demonstrated that valve design was a major determinant of the durability of pericardial xenografts.

To overcome some of the problems related to prosthetic valve design, a new pericardial bioprosthesis was developed by Meadox Medicals and presented by Gabbay and Frater in 1982 [17]. This valve was made of a single leaflet of glutaraldehyde-fixed bovine pericardium mounted on a flexible Delrin stent covered by pericardium to avoid the abrasive meeting of cloth and bioprosthetic tissue [1]. Moreover, taking advantage of the wide opening of the unicusp, this particular design was conceived to allow a favorable ratio between the internal and external diameters; this resulted in improved hemodynamic performance, especially in the smaller sizes, as demonstrated by extensive in vitro tests [1]. Wide and continuous movement of the single leaflet was also considered important in reducing the amount or delaying the onset of tissue fibrosis and ultimate calcification [1].

Based on these observations we, together with other European researchers, started a clinical trial with this device in 1983. However, despite an encouraging multicenter preliminary experience [2], follow-up of our patients has shown that the Meadox-Gabbay valve has not met the initial expectations. In fact, of 12 patients who received this device at our institution, only 4 (25%) still have the original unicusp bioprosthesis in place after a maximum follow-up of approximately 7 years. Five patients required reoperation for prosthetic valve failure, and 3 died of cardiac failure without reoperation. Two of the deaths were possibly related to valve dysfunction.

Our pathological findings are in agreement with those reported by Shemin and colleagues [3] in an experimental animal model. All five explants available for pathological evaluation in our series showed redundancy and stretching of the single leaflet, and in one instance, this lesion was so severe as to cause by itself hemodynamically

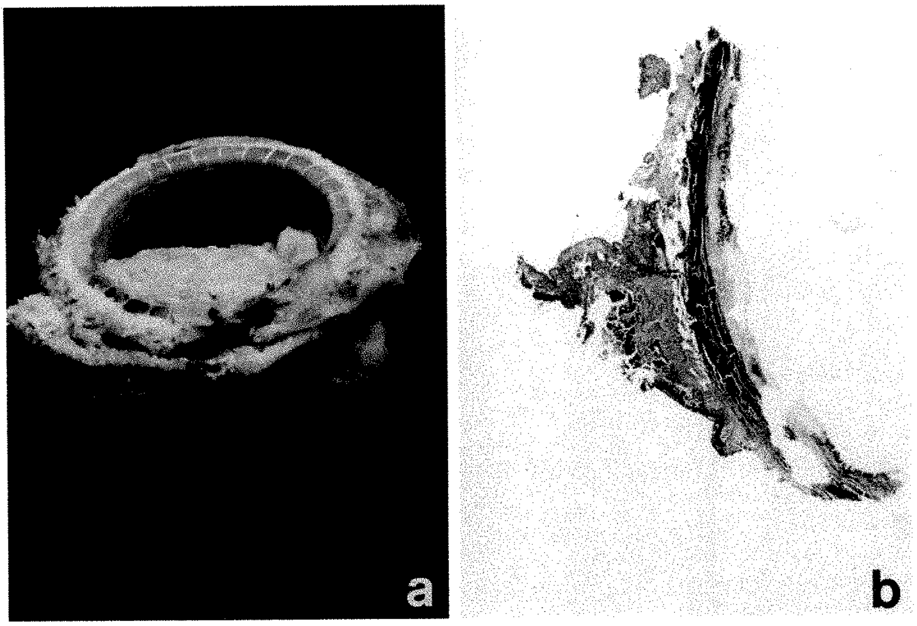


Fig 4. (Patient 9.) Pericardial xenograft explanted after 22 months because of infective endocarditis. Vegetations are visible at both (a) gross examination and (b) histologic examination. (Azan; ×10 before 22% reduction.)

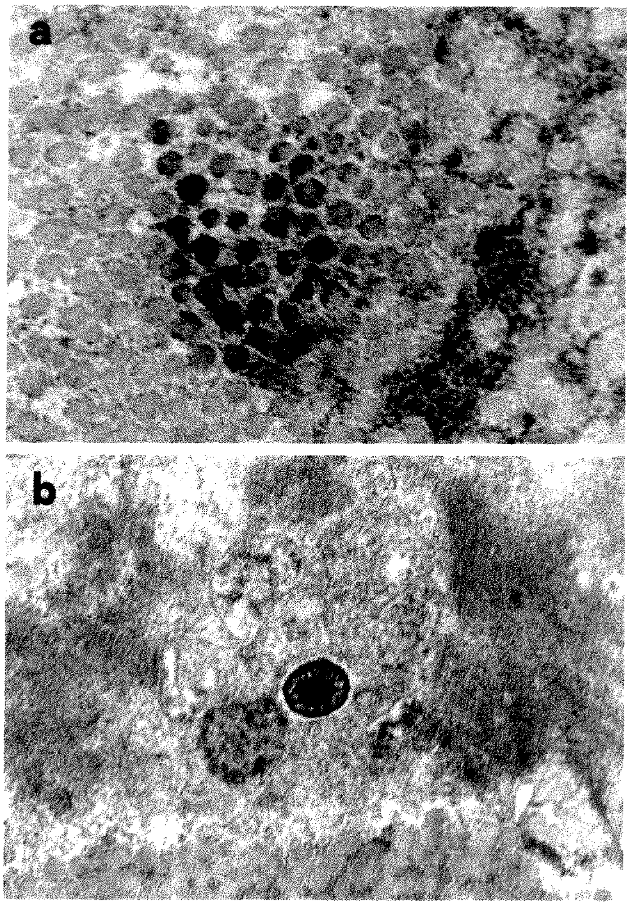


Fig 5. (Patient 1.) Electron micrographs showing calcifications involving both (a) collagen fibers and (b) cellular debris. (Uranyl acetate and lead citrate; a, ×48,000, and b, ×30,000, both before 20% reduction.)

significant regurgitation. The cause of pericardial stretching is not yet fully understood. This problem, which has also been observed occasionally in other pericardial bioprostheses [10, 13], could be due to heterogeneity of the mechanical properties of bovine pericardium with the result that different areas of the same tissue exhibit different degrees of extensibility [10, 18]. This phenomenon is most likely exacerbated in the unicusp design [19]. It is noteworthy that it has not been observed to date in another new pericardial valve that comprises a single three-cuspal molded pericardial sheet (Pericarbon; Sorin Biomedica, Saluggia, Italy) [20]. Quality control of the tissue appears to be another major factor affecting durability of pericardial xenografts [21].

Dystrophic calcification was the cause of failure in three explants, demonstrating that even wide and continuous movement of the single cusp does not prevent this complication. The morphology of calcification in glutaraldehyde-tanned pericardial xenografts has been shown to be strikingly similar to that occurring in porcine bioprostheses [22], although porcine aortic and pericardial tissues exhibit several differences from the structural point of view [23]. Trowbridge and associates [12] pointed out that mineralization is the result of tissue disruption caused by flexural stresses; in fact, they observed that calcification always starts at the boundary between the undamaged tissue and the site of collagen breakdown and that calcification is never present without collagen disruption. Mechanical stress is therefore confirmed as an important determinant of tissue calcification, as also observed in our series. However, the finding in one of our explants that calcification can occur also in the pericardium covering the stent indicates that tissue preservation and treatment play an important role as well.

Cellular infiltrates have been reported to occur within pericardial bioprostheses [10] and were observed focally in all but one of our specimens. Except for one instance in which they were related to valve infection, the infiltrates in the other explants can be considered a consequence of an immunological reaction to pericardial tissue. Whether this might favor calcific degeneration is still controversial.

In conclusion, various modes of failure have been observed in Meadox-Gabbay pericardial xenografts implanted in the mitral position that greatly reduce the durability of this device. Despite a limited experience, in terms of both number of patients and length of follow-up, it appears that use of the unicusp principle in the manufacture of valves has failed to provide a reliable pericardial bioprosthesis.

Supported by National Council for Research, Target Projects "Aging" and "BT.BS.", Rome and Milan, Italy.

References

1. Gabbay S, Bortolotti U, Cipolletti G, Wasserman F, Frater RWM, Factor SM. The Meadox unicusp pericardial bioprosthetic heart valve: new concept. Ann Thorac Surg 1984;37:448–56.
2. Soots G, Cabrol C, Gandjbakhch I, et al. Preliminary clinical results with Meadox-Gabbay unicusp pericardial heart valve bioprosthesis. In: Bodnar E, Yacoub M, eds. Biologic and bioprosthetic valves. New York: Yorke Medical Books, 1986:699–708.
3. Shemin RJ, Schoen FJ, Hein R, Austin J, Cohn LH. Hemodynamic and pathologic evaluation of a unileaflet pericardial bioprosthetic valve. J Thorac Cardiovasc Surg 1988;95:912–9.
4. Gallucci V, Mazzucco A, Bortolotti U, Milano A, Guerra F, Thiene G. The standard Hancock porcine bioprosthesis: overall experience at the University of Padova. J Cardiac Surg 1988;3(Suppl):337–45.
5. Milano A, Bortolotti U, Talenti E, et al. Calcific degeneration as the main cause of porcine bioprosthetic valve failure. Am J Cardiol 1984;53:1066–70.
6. Valente M, Bortolotti U, Thiene G. Ultrastructural substrates of dystrophic calcification in porcine bioprosthetic valve failure. Am J Pathol 1985;119:12–21.
7. Ionescu MI, Tandon AP, Silverton NP, Chidambaram M, Smith DR. Long-term durability of the pericardial valve. In: Bodnar E, Yacoub M, eds. Biologic and bioprosthetic valves. New York: Yorke Medical Books, 1986:165–76.
8. Becker RM, Strom J, Frishman W, et al. Hemodynamic performance of the Ionescu-Shiley prosthesis. J Thorac Cardiovasc Surg 1980;80:613–20.
9. Gabbay S, Bortolotti U, Wasserman F, Factor S, Strom J, Frater RWM. Fatigue-induced failure of the Ionescu-Shiley pericardial xenograft in the mitral position. In vivo and in vitro correlation and a proposed classification. J Thorac Cardiovasc Surg 1984;87:836–44.

10. Schoen FJ, Fernandez J, Gonzalez-Lavin L, Cernaianu A. Causes of failure and pathologic findings in surgically removed Ionescu-Shiley standard bovine pericardial heart valve bioprostheses: emphasis on progressive structural deterioration. Circulation 1987;76:618–27.
11. Walley VM, Keon WJ. Patterns of failure in Ionescu-Shiley bovine pericardial bioprosthetic valves. J Thorac Cardiovasc Surg 1987;93:925–33.
12. Trowbridge EA, Lawford PV, Crofts CE, Roberts KM. Pericardial heterografts. Why do these valves fail? J Thorac Cardiovasc Surg 1988;95:577–85.
13. Thiene G, Bortolotti U, Valente M, et al. Mode of failure of the Hancock pericardial valve xenograft. Am J Cardiol 1989; 63:129–33.
14. Bortolotti U, Milano A, Thiene G, et al. Early mechanical failures of the Hancock pericardial xenograft. J Thorac Cardiovasc Surg 1987;94:200–7.
15. Bortolotti U, Milano A, Mazzucco A, et al. The Hancock pericardial xenograft: incidence of early mechanical failure at a medium-term follow-up. Eur J Cardiothorac Surg 1988;2: 458–62.
16. Bortolotti U, Milano A, Guerra F, et al. Failure of Hancock pericardial xenografts: is prophylactic bioprosthetic replacement justified? Ann Thorac Surg 1991;51:430–7.
17. Gabbay S, Frater RWM. The unileaflet heart valve bioprosthesis: new concept. In: Cohn LH, Gallucci V, eds. Cardiac bioprostheses. New York: Yorke Medical Books, 1982:411–24.
18. Trowbridge EA, Roberts KM, Crofts CE, Lawford PV. Pericardial heterografts. Toward quality control of the mechanical properties of glutaraldehyde-fixed leaflets. J Thorac Cardiovasc Surg 1986;92:21–8.
19. Black MM, Drury PJ, Lawford PV, Howard IC, Patterson EA. Advantages and disadvantages of uni- and multi-leaflet tissue valve configurations. In: Bodnar E, ed. Surgery for heart valve disease. London: ICR Publishers, 1990:755–64.
20. Thiene G, Laborde F, Valente M, et al. Morphological survey of a new pericardial valve prosthesis (Pericarbon): long-term animal experimental model. Eur J Cardiothorac Surg 1989;3: 65–74.
21. Valente M, Laborde F, Thiene G, et al. Evaluation of Pericarbon valve prosthesis. In vitro, ultrastructural, and animal studies. J Cardiac Surg 1989;4:79–88.
22. Schoen FJ, Tsao JW, Levy RJ. Calcification of bovine pericardium used in cardiac valve bioprostheses. Implications for the mechanisms of bioprosthetic tissue mineralization. Am J Pathol 1986;123:134–45.
23. Allen DJ, DiDio LJ, Zacharias A, et al. Microscopic study of normal parietal pericardium and unimplanted Puig-Zerbini pericardial valvular heterografts. J Thorac Cardiovasc Surg 1984;87:845–55.

INVITED COMMENTARY

Dr Bortolotti and colleagues are to be commended for this interesting clinical follow-up of a very small cohort of 12 patients with the prototype version of the unileaflet heart valve bioprosthesis. The conclusions of this article are misguided, however, because the reader does not have the opportunity to see the whole picture. The subtitle *Failure of the Unicusp Principle* sets the tone. I fail to understand on what basis Bortolotti and colleagues have condemned this interesting principle, which is doing very well in nature at least. For example, the turtle has a unicusp mitral valve that can last several hundred years. To be successful, our aim must be to imitate nature as closely as possible. The development, the preclinical trials, and the research performed, as well as a small series of multicenter clinical implantations, were most rewarding in terms of understanding how pericardial valves fail and how their durability can be substantially improved. Although Bortolotti and colleagues were aware of the research done immediately after the clinical study was discontinued [1], they did not mention or elaborate on the outcome of this research. It is unfortunate that the scope of this article did not include what we have learned and how we have solved the problems seen in this very small clinical series. By printing only half of the truth, we will never reach the scientific objective of making better valves.

The unileaflet valve was developed with the intention of improving the hemodynamic properties of heart valve bioprostheses, especially small prostheses, as well as to reduce the rate of calcification caused by mechanical factors. Canine studies [2] demonstrated that a single moving cusp can resist calcification better than a nonmoving or sluggishly moving leaflet.

Although we found out that the pericardium covering the stent generally does not calcify, this has a different explanation—an explanation could be that only the smooth surface of the pericardium is in contact with the blood. Furthermore, normal exchange of nutrients is disturbed by the dividing plastic material of the stent. The selection of the pericardial tissue and the preclinical bench testing were done using the technology available in 1980, but later we realized that some valves had failed earlier than we had expected. Although it was too early to know the long-term outcome, we elected to stop clinical implantation and immediately started a thorough research program, mostly to understand the problems of redundancy and early tears.

The results of this research have been published [1] and are fascinating. First, it was found that the pericardial fibers were textured in a certain direction based on the axis of the bovine pericardial sac with the short axis (or circumference) being substantially more extensible. If the cusp of the unileaflet valve has the circumferential direction fixed from one edge of the stent to the other, this cusp will be prone to stretching and eventual redundancy. If the long-axis direction is used, the cusp will maintain its integrity much longer.

Second, we learned that although the tissue macroscopically looks acceptable during histologic sectioning, most of the pericardial sac tissue has clear signs of degeneration and only one or two areas (if any) have a dense structure that can withstand the wear and tear necessary for cusp material. We realized that each individual cusp must pass the microscopic test before it can be used as cusp tissue. We also found that some pericardial tissue is hyperextensible and can elongate more than 100% of its original length before rupturing in the tester. Variability is a key problem for handmade valves.

Finally, we found that the sharp edges of the stent had to be modified to absorb shock in optimal fashion. None of these facts were known or sufficiently appreciated in 1983 when the first valve was implanted in patients.

These improvements made the new unileaflet valve five times more resistant to failure in the durability testers. These quality-control points, and the wide variability of the pericardial tissue, are substantiated by the fact that 30% of the patients are doing very well and the echocardiograms show a normal valve after 8 years. By learning how to optimize the quality of the valve to resemble the valves that did very well in the clinical test, we can probably make a durable valve. The key factor is to find a method to reduce variability to an absolute minimum. It is also worthy of note that in a patient with renal failure, the bioprosthesis tends to calcify as early as a month or 2 after implantation, whereas in this series, the valve in patient 12 did not calcify until 31 months. Although to include this patient in the study was a protocol violation, it was interesting that the valve did calcify more slowly as seen in preclinical studies. I must stress that some biological factors are certainly at play but are not within the scope of this commentary. Because of the difficulties involved in introducing changes in any heart valves owing to the government regulatory process and the perceived liability, the manufacturer of this valve elected not to proceed and perform clinical studies with the new valve.

Based on new designs introduced to clinical use, it is clear that pericardial valves have a future because of some obvious advantages. A comeback is probable, and the unileaflet valve might one day get a second chance. In my laboratory, I have a heart that was explanted from a 300-year-old turtle. The unicusp principle does work. It is a more appropriate design for the mitral position, and the technology is now available to make this valve durable.

Shlomo Gabbay, MD

Department of Cardiothoracic Surgery
UMDNJ, New Jersey Medical School
185 S Orange Ave, Rm G502
Newark, NJ 07103

References

1. Gabbay S, Welch H. Reducing the variability in durability of heart valve bioprostheses. Am Soc Artif Organs J 1988;34:1022–6.
2. Gabbay S, Bortolotti U, Cipolletti G, Wasserman F, Frater RWM, Factor SM. The Meadox unicusp pericardial bioprosthetic heart valve: new concept. Ann Thorac Surg 1984;37:448–56.

Comparison of Cardiac Output Measured by Intrapulmonary Artery Doppler, Thermodilution, and Electromagnetometry

Paul M. Heerdt, MD, PhD, Charles G. Pond, MD, George A. Blessios, MD, and
Michael Rosenbloom, MD

Section of Cardiothoracic Anesthesia and Division of Cardiothoracic Surgery, Washington University School of Medicine, St. Louis, Missouri

A Doppler pulmonary artery catheter system (Doppler cardiac output monitor or DOPCOM) that continuously measures instantaneous and mean cardiac output was recently introduced. Because thermodilution (TD) flow measurements may not represent an adequate standard, the present study was designed to compare TD and DOPCOM cardiac output measurements with aortic electromagnetic (EM) flow in cardiac surgical patients. Twenty-one patients scheduled for elective coronary artery bypass grafting were enrolled in the study. Simultaneous measurement of cardiac output by all three methods was performed before cardiopulmonary bypass, after cardiopulmonary bypass with the aorta cannulated and volume intermittently infused, and after decannulation. Analysis of all data demonstrated fair TD and EM correlation (r = 0.80), with minimal bias (0.03 ± 1.21 L/min) and a median absolute error of 0.53 L/min; DOPCOM and EM data showed moderate correlation (r = 0.64), a bias of −0.61 ± 1.50 L/min, and a median absolute error the same as TD (0.51 L/min). However, distribution of DOPCOM values was heavily skewed by 3 patients in whom flow measurements immediately after cardiopulmonary bypass were markedly different between the DOPCOM and electromagnetometry, probably because of malposition of the Doppler transducers secondary to partial catheter withdrawal during bypass. Consistent with this theory was the finding that before CPB, the DOPCOM was significantly better than TD in predicting EM flow (median absolute error: DOPCOM, 0.12 L/min, and TD, 0.48 L/min; p = 0.04). Our data suggest that, in general, the DOPCOM shows similar precision to TD for predicting EM flow measurements, although the DOPCOM may underestimate actual flow. However, when optimal position of the DOPCOM catheter is maintained, the device is significantly more precise than TD and does not underestimate flow. Furthermore, the instantaneous on-line data provided by the DOPCOM may potentially provide the basis for beat-to-beat assessment of the pulmonary circulation and right ventricular function.

(Ann Thorac Surg 1992;54:959–66)

A Doppler pulmonary artery (PA) catheter system (Doppler cardiac output monitor or DOPCOM) capable of continuously measuring space-averaged PA blood flow-velocity and cross-sectional area, and calculating beat-to-beat flow, was recently introduced. Previous investigation has indicated excellent correlation of this method with electromagnetic (EM) flow measurements in pump models and animals [1] and with Fick determination of cardiac output in humans [2]. However, although recent comparison of the DOPCOM with conventional thermodilution (TD) measurements of flow in surgical patients demonstrated a moderately strong correlation, there was distinct variability between the methods [3].

Clinically, TD measurement of cardiac output is subject to a variety of errors and can vary widely from both dye-dilution and Fick measurements of flow [4, 5]. Thus, TD may not be an adequate standard for the evaluation of new flow technology in the perioperative setting. Electromagnetic measurement of aortic blood flow has long been used as the laboratory "gold standard" for cardiac output measurement. Other than probe placement and appropriate calibration, this continuous method requires no operator intervention, and although the small amount of blood perfusing the coronary circulation is not measured, it correlates closely with direct volume measurements of flow. Using electromagnetometry, we [6] recently observed marked overestimation of cardiac output by TD after the acute onset of tricuspid regurgitation in a patient undergoing a cardiac operation.

The present study was designed first to confirm TD capabilities of the Doppler PA catheter (which also contains a thermistor) under controlled laboratory conditions in open chest dogs and then to compare simultaneous determinations of cardiac output by TD, DOPCOM, and aortic electromagnetometry before and after cardiopulmonary bypass (CPB) in cardiac surgical patients.

Accepted for publication June 4, 1992.

Address reprint requests to Dr Heerdt, Department of Anesthesiology, Washington University School of Medicine, 660 S Euclid, Box 8054, St. Louis, MO 63110.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

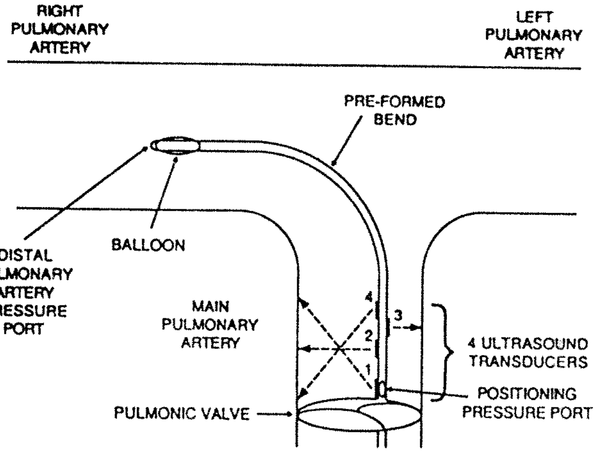


Fig 1. The Flocath: location and orientation of ultrasonic transducers, the positioning port, and the preformed bend approximately 9 to 10 cm from the tip to facilitate optimal transducer positioning. The function of ultrasound transducers 1 and 4 is to measure velocity of red blood cells; the function of transducers 2 and 3 is to measure the diameter of the main pulmonary artery. (Used by permission of Cardiometrics, Inc, Mountain View, CA.)

Material and Methods

Doppler Catheter

All studies were performed with a 7.5F PA catheter equipped with four 10-MHz ultrasonic transducers 12 to 13 cm from the distal tip (Flocath; Cardiometrics, Inc, Mountain View, CA) (Fig 1). The catheter is preformed with a slight bend distal to the transducers to facilitate optimal positioning with the tip in the right branch of the PA. In contrast to previous studies [2, 3], an internal guidewire was not used to straighten the bend during catheter placement. The Flocath is otherwise similar to standard PA catheters except for a "positioning port" next to the transducers to aid in verifying placement in the PA and not the right ventricular outflow tract.

Instantaneous cardiac output (Q) is derived from the following formula: $Q = \text{Area} \times V_{SA}$, where Area = cross-sectional area of the PA and V_{SA} = space-averaged blood velocity measured in the same plane as area. Using this formula, instantaneous volume-flow is calculated every 30 ms by the DOPCOM (Cardiometrics, Inc) and digitally displayed as either peak or mean flow.

The theory and methods by which the DOPCOM accurately measures cross-sectional area and velocity have been extensively presented elsewhere [1, 2]. Briefly, functioning as a multirange-gate pulsed Doppler velocimeter, the DOPCOM constructs a one-dimensional velocity profile using six individual range gates spanning the PA diameter. Instantaneous blood velocity at each of the gates is calculated by the Doppler equation. Angle-positioning errors resulting from nonparallel alignment of the catheter's long axis and blood flow–velocity vector are determined by two transducers oriented to emit ultrasound beams at different angles to the vessel wall (see Fig 1). Should angle error be detected, true instantaneous blood velocity at each gate is calculated by incorporating the magnitude of this error into the Doppler equation. Using a model that assumes hemisymmetric three-dimensional flow profiles within the PA, instantaneous space-averaged velocity is calculated by multiplying individual velocities by a variable area weighing factor based on location of range gates in the vessel and then summing all the products. Simultaneously, PA diameter (D) is determined by measuring the distance of the catheter from the front and back walls of the vessel by ultrasonic transit time from two transducers located on the front and back surfaces of the catheter (see Fig 1), adding these distances to the catheter width, and multiplying by the calculated angle error. Cross-sectional area of the PA is then calculated based on the assumption that the PA just distal to the pulmonary valve is cylindrical (area = $\pi D^2/4$). Waveforms depicting space-averaged velocity, diameter change, and flow can be continuously displayed, essentially in real-time (Fig 2).

Animal Studies

Under a protocol approved by our institutional animal studies committee, 4 dogs weighing 25 to 30 kg were used for the control experiments. They were anesthetized with sodium thiopental, sodium pentobarbital, and fentanyl. After induction of anesthesia, tracheal intubation, and initiation of mechanical ventilation with 100% oxygen, the left femoral artery was cannulated for blood pressure measurement, and a Flocath was inserted through the right external jugular vein. Then the left femoral artery and vein were isolated and cannulated with a single large-bore Silastic (Dow Corning, Midland, MI) catheter to create an arteriovenous shunt; this catheter was kept clamped until a specific point in the protocol. A median sternotomy was then performed, the pericardium opened, and a sling constructed.

To assure that cold injectate was administered into the right atrium in exactly the same fashion each time, a second Flocath, which had been transected just distal to the injection port, was inserted directly into the right atrium and secured with a pursestring suture. An EM flow probe (model SF 245, 250, or 255; Carolina Medical Instruments, Inc, King, NC) was then placed around the ascending aorta for measurement of cardiac output (model 701D flowmeter; Carolina Medical Instruments, Inc). Before measurements were made, blood hematocrit was determined and the appropriate probe factor verified. Animals were warmed with heating lamps, and body temperature was maintained between 36.5° and 37.5°C.

After a 10-minute stabilization period, multiple simul-

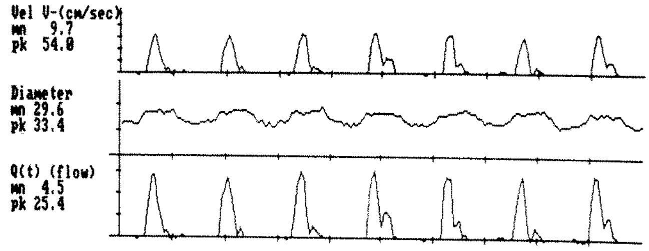


Fig 2. Tracing depicting beat-to-beat space-averaged pulmonary arterial blood velocity, diameter, and blood flow. (mn = *mean;* pk = *peak.)*

taneous measurements of cardiac output were performed, first under baseline conditions, then with the arteriovenous shunt open to increase cardiac output, and then during 2.5% halothane inhalation to decrease cardiac output. All TD cardiac outputs were determined with an American Edwards cardiac output computer (model 9250) using 10 mL of 5% dextrose solution at room temperature (23° to 24°C) injected into the catheter positioned directly in the right atrium. Indicator was administered by the same person each time during apnea at end-expiration. Values were compared with the EM measurement digitally displayed at the moment of indicator injection. Because the transducers could not be advanced out of the right ventricle in most dogs without placing the distal tip of the catheter in permanent wedge position, DOPCOM flow measurements were not recorded.

Clinical Protocol

After the protocol was approved by our institutional human studies committee, 21 patients scheduled for elective coronary artery bypass grafting were enrolled in the study. In all but 2 patients, the Flocath was placed through the right external jugular vein before induction of anesthesia. If persistent ventricular arrhythmias occurred or the catheter could not be positioned properly, the patient was excluded from the study and a conventional PA catheter placed.

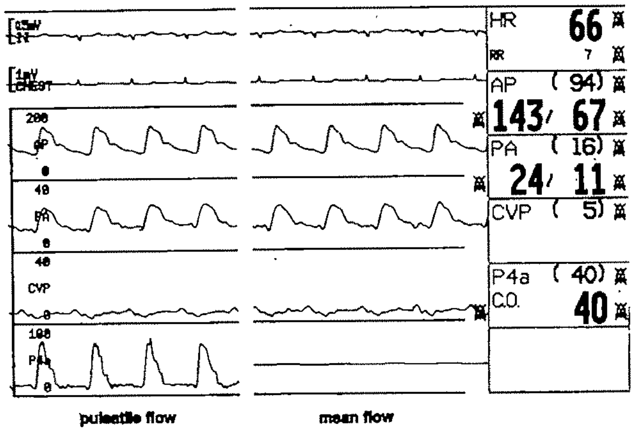


Fig 4. Tracings of pulsatile and mean pulmonary artery blood flow along with other hemodynamic variables as they appear on operating room monitors. (AP = *radial arterial pressure in millimeters of mercury;* CVP = *central venous pressure in millimeters of mercury;* HR = *heart rate;* PA = *pulmonary artery pressure in millimeters of mercury;* P4a = *pressure channel No. 4 scaled so that 100 mm Hg equals 30 L/min pulsatile flow or 10 L/min mean flow, and thus, the reading of 40 shown represents a cardiac output* [C.O.] *of 4.0 L/min.)*

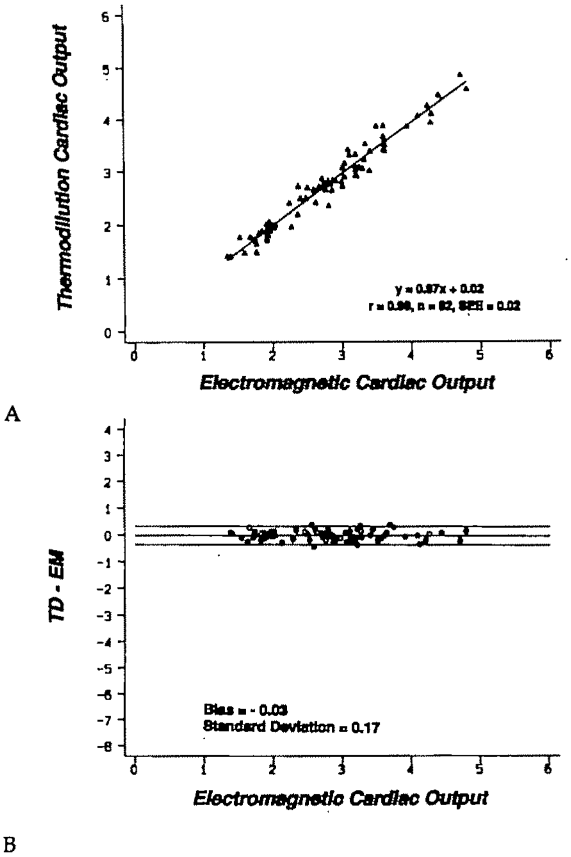


Fig 3. Animal control: (A) linear regression of thermodilution cardiac output plotted as a function of aortic electromagnetic flow and (B) the thermodilution – electromagnetic difference (TD – EM) *for each measurement plotted as a function of electromagnetic flow to determine mean bias and limits of agreement (2 standard deviations from the mean bias). Data were obtained under closely controlled conditions in anesthetized dogs.*

Patients were anesthetized with opiate and lorazepam, and vecuronium bromide was used for relaxation. After tracheal intubation, a transesophageal echocardiographic probe was inserted into the esophagus (unless the patient had been heparinized preoperatively) to assess valve function and regional wall motion, as well as to attempt to verify placement of the Flocath in the right PA. After sternotomy and opening of the pericardium, an EM flow probe (model SF 280, 285, or 290; Carolina Medical Instruments, Inc) was placed around the ascending aorta after hematocrit measurement and automatic computation of the probe factor. If an adequate probe fit could not be attained, the patient was excluded from the study. Flow probes used were new, and accuracy was confirmed by comparison with direct volumetric measurement of flow before and on completion of the study.

Simultaneous cardiac output measured by TD, DOPCOM, and electromagnetometry (model 701D flowmeter; Carolina Medical Instruments, Inc) was performed before CPB, after weaning from CPB with the aorta still cannulated and volume intermittently infused, and after decannulation of the aorta. For measurements after CPB, EM flow probes were placed distal to vein grafts and proximal to the aortic cannulation site after hematocrit measurement and automatic computation of the probe factor. Thermodilution cardiac output was measured with an Oximetrix 3 cardiac output computer (Abbott Laboratories, North Chicago, IL) using 10 mL of room-temperature injectate administered by the same person each time during apnea at end-expiration; values were recorded along with DOPCOM and EM flows digitally displayed at

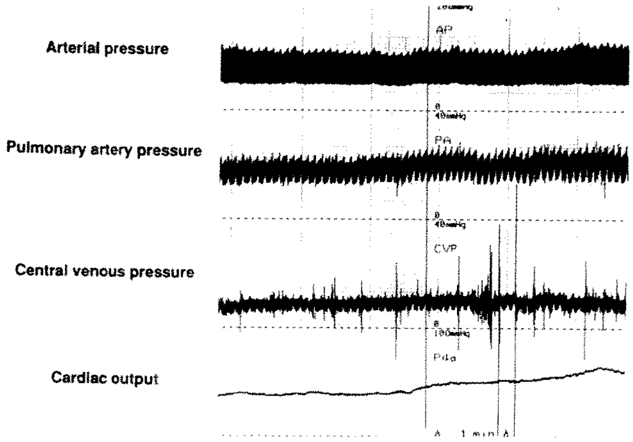


Fig 5. Tracing depicting a progressive increase in cardiac output in response to volume infusion. Abbreviations are the same as in Figure 4.

the moment of injection. For all methods, the average of three readings was regarded as the final value.

Data were analyzed by conventional linear regression, the method comparison procedures described by Altman and Bland [7], and the predictive performance tests described by Sheiner and Beal [8]. Calculated p values of less than 0.05 were regarded as significant.

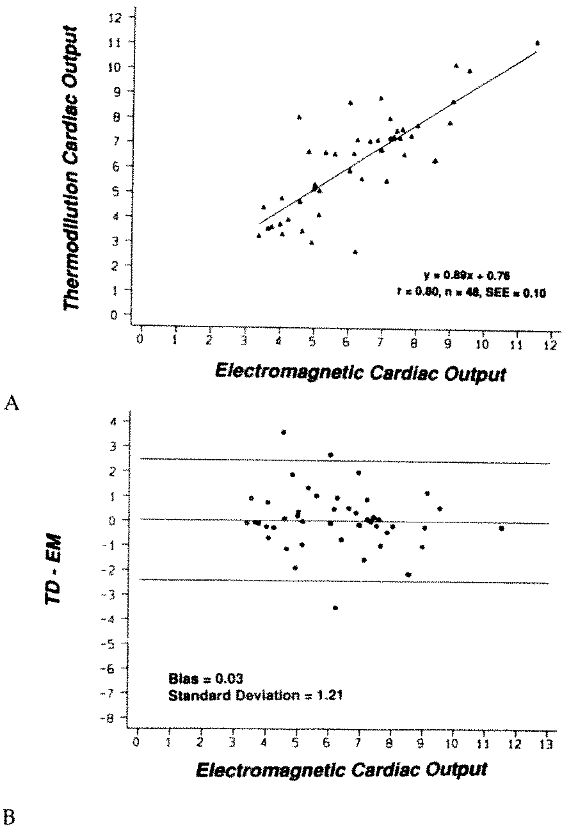


Fig 6. Patient studies: (A) linear regression of thermodilution cardiac output plotted as a function of aortic electromagnetic flow and (B) the thermodilution – *electromagnetic difference* (TD – EM) *for each measurement plotted as a function of electromagnetic flow to determine mean bias and limits of agreement (2 standard deviations from the mean bias). Data obtained at all three time points are presented.*

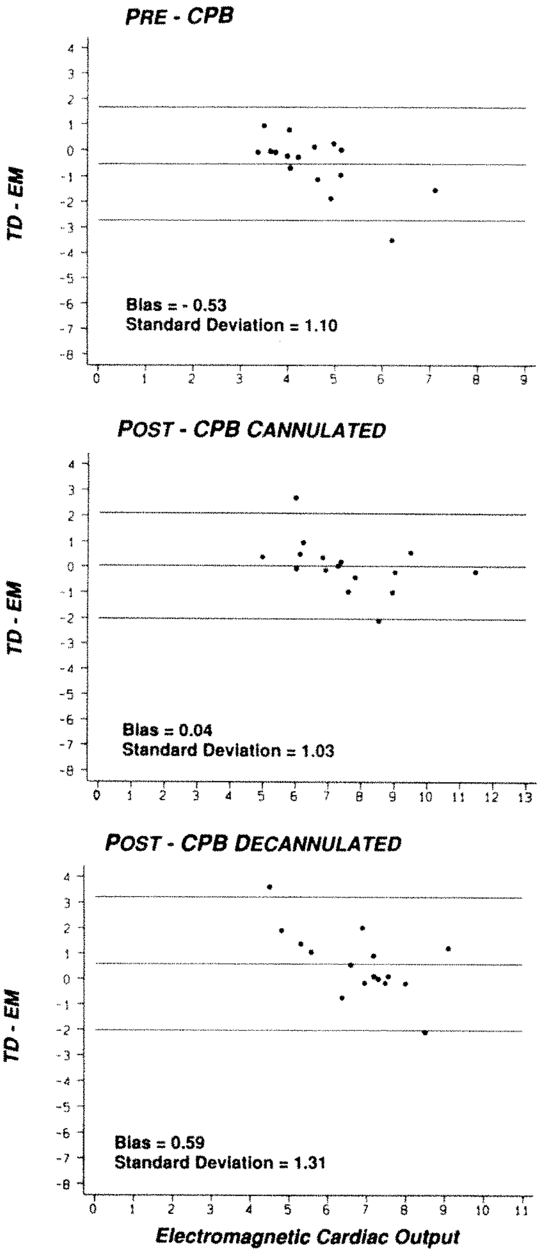


Fig 7. The thermodilution – *electromagnetic difference* (TD – EM) *plotted as a function of electromagnetic flow to determine bias and limits of agreement for measurements obtained at each of the three time points: before cardiopulmonary bypass* (PRE-CPB)*; after CPB with aortic perfusion cannula in place* (POST-CPB CANNULATED)*; and after CPB with aortic perfusion cannula removed* (POST-CPB DECANNULATED.)

Results

Animal Studies

Linear regression of TD and EM flows ranging from 1.2 to 4.8 L/min in the dog is shown in Figure 3. Under these closely controlled conditions, there is excellent correlation

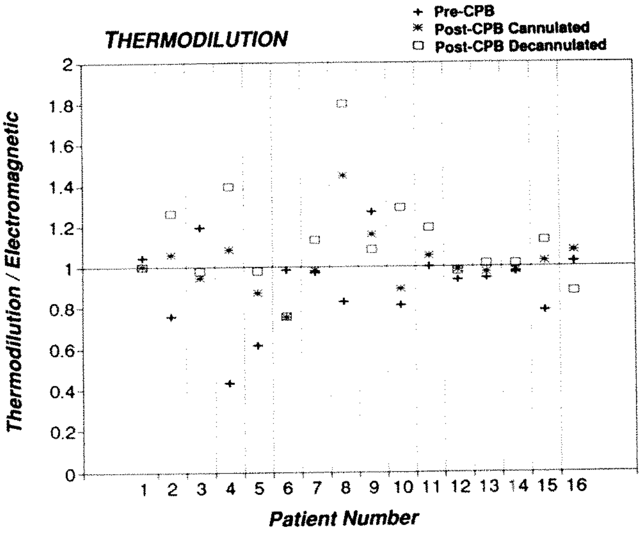


Fig 8. Relative accuracy of thermodilution cardiac output measurements (thermodilution/electromagnetic ratio) for each patient at each of the three time points. Patients 4, 6, and 8 had intraoperative echocardiographic evidence of tricuspid regurgitation. Abbreviations are the same as in Figure 7.

between the two methods, with minimal bias (the mean TD − EM difference) and narrow limits of agreement (2 standard deviations from the mean TD − EM difference).

Patient Studies

Of the 21 patients enrolled in the study, 5 were excluded: 1 because the Flocath could not be properly positioned (a female patient weighing 41 kg), 1 because of persistent ventricular ectopy (which recurred after replacement of the catheter with a conventional PA catheter), and 3 because of inadequate fit of the EM flow probe. Nearly half of the patients included in the full protocol (7/16) displayed transient ventricular ectopy during placement of the catheter.

Continuous flow data from the DOPCOM (either mean or pulsatile) were entered into the operating room monitor system by way of a standard pressure amplifier, scaled with an analog calibration signal, and continuously recorded on a strip chart. For the study, scales were set such that 100 mm Hg on the pressure channel equaled 30 L/min of pulsatile flow and 10 L/min of mean flow. Thus, when monitoring mean flow, a reading of 40 mm Hg on the monitor represented a cardiac output of 4.0 L/min. Representative tracings of hemodynamic variables and PA flow as they appeared on the operating room monitor and strip chart are shown in Figures 4 and 5, respectively.

Comparison of TD and EM flow is shown in Figure 6. A fair correlation is evident, with flows ranging from 3.5 to 12 L/min. However, although there is no apparent bias, the limits of agreement are relatively wide, and data points are diffusely scattered. Breaking data down into the three time points does not reveal a marked difference between values obtained before and after CPB (Fig 7). However, relative accuracy (expressed as the TD/EM ratio) for each patient at each time point demonstrates that patients 4 and 8 had the poorest relative accuracy between the three time points (Fig 8). Both of these patients, along with patient 6, displayed intraoperative transesophageal echocardiographic evidence of tricuspid regurgitation. If their data are removed, TD and EM correlation improves ($r = 0.92$), the bias is negligible (0.03 L/min), and the limits of agreement are narrow (1.58 L/min) (Fig 9).

Comparison of DOPCOM and EM flow is shown in Figure 10. Correlation ($r = 0.64$), bias (−0.61 L/min), and limits of agreement (3.0 L/min) are clearly influenced by a few prominent "outliers," with the remaining data points closely grouped. Breaking data down into the three time points reveals that after CPB when the aorta is still cannulated and volume has been infused, there is a substantial difference between DOPCOM and EM flow (Fig 11). However, this disparity diminishes after the aorta is decannulated. If data obtained with the aorta cannulated are omitted, correlation markedly improves and the limits of agreement are narrowed substantially (Fig 12). Relative accuracy of DOPCOM measurements (the DOPCOM/EM ratio) for each patient is shown in Figure 13. During the period of cannulation after CPB, patients 7, 10, and 15 displayed DOPCOM/EM ratios of less than 0.5. Unlike the tricuspid regurgitation that was

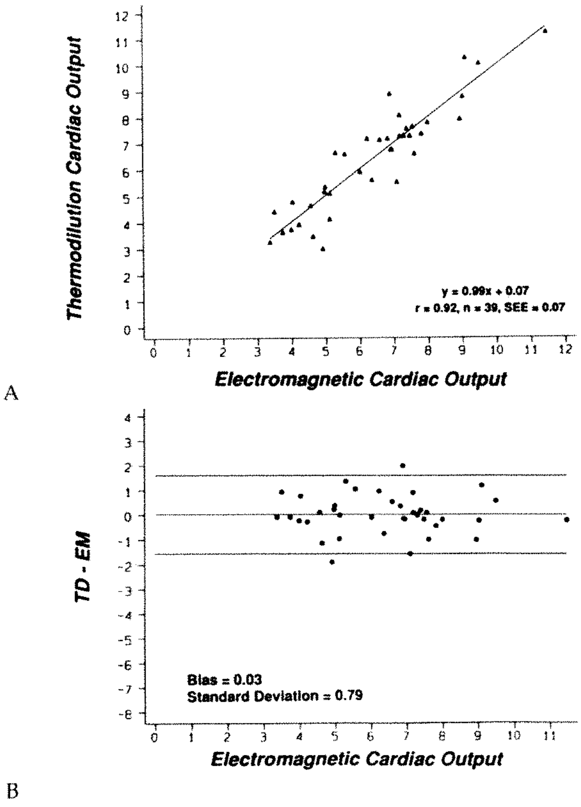


Fig 9. (A) Linear regression of thermodilution cardiac output plotted as a function of aortic electromagnetic flow and (B) the thermodilution − electromagnetic difference (TD − EM) for each measurement plotted as a function of electromagnetic flow to determine mean bias and limits of agreement (2 standard deviations from the mean bias). Data from patients with echocardiographic evidence of tricuspid regurgitation were excluded.

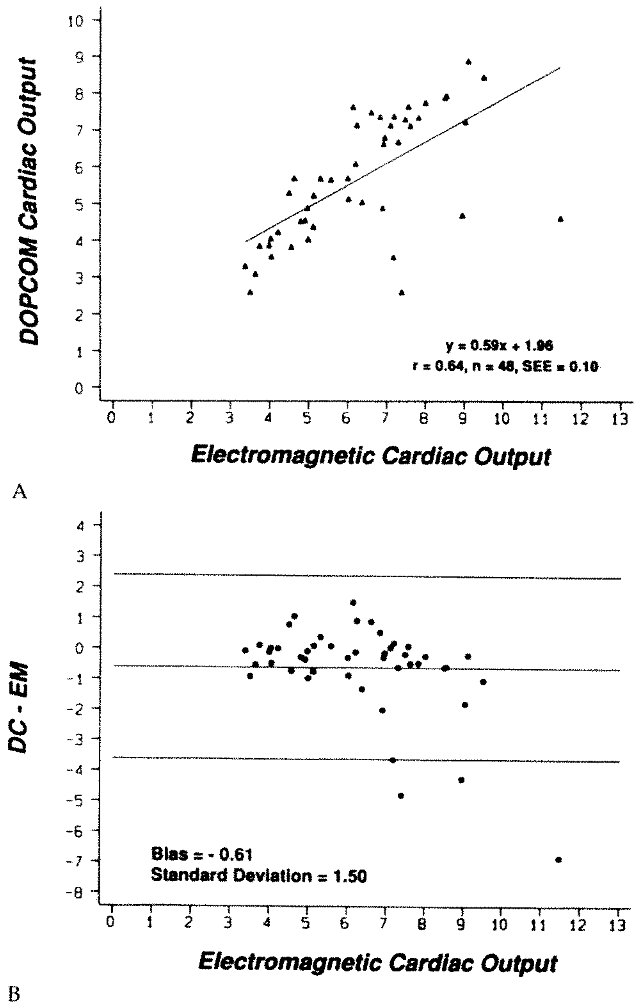


Fig 10. (A) Linear regression of Doppler cardiac output monitor (DOPCOM) cardiac output plotted as a function of aortic electromagnetic flow and (B) the DOPCOM − electromagnetic difference (DC − EM) for each measurement plotted as a function of electromagnetic flow to determine mean bias and limits of agreement (2 standard deviations from the mean bias). All data obtained at all three time points are presented.

evident on transesophageal echocardiography and apparently influenced TD measurements, no specific or consistent factor was immediately apparent in these patients to account for the variability during the cannulation period after bypass. However, chest radiographs obtained postoperatively revealed that in 2 of the patients (patients 10 and 15), the Flocath was suboptimally positioned in the left PA despite previous transesophageal echocardiographic indication of placement in the right PA. Whether the catheter was in a similar position when readings were obtained after CPB is uncertain.

Because a few patients displayed TD or DOPCOM values that were markedly different from EM values, thus skewing distribution of mean data, median differences in precision and bias were quantitated and analyzed by the methods described by Sheiner and Beal [8]. When all time points are considered together, TD and the DOPCOM are identical in terms of precision but different with respect to bias (Table 1). When data are broken down into individual time points, the DOPCOM is more precise than TD before CPB, and the two methods display similar bias. However, after CPB with the aorta cannulated, there is no significant difference in precision (although the value for TD is less than half that for the DOPCOM) but a marked difference in bias. After decannulation of the aorta, there is no significant difference in precision of the two methods, although the value for the DOPCOM is less than half that for TD. However, the difference in bias remains, although it now appears to be primarily the result of an increased TD value.

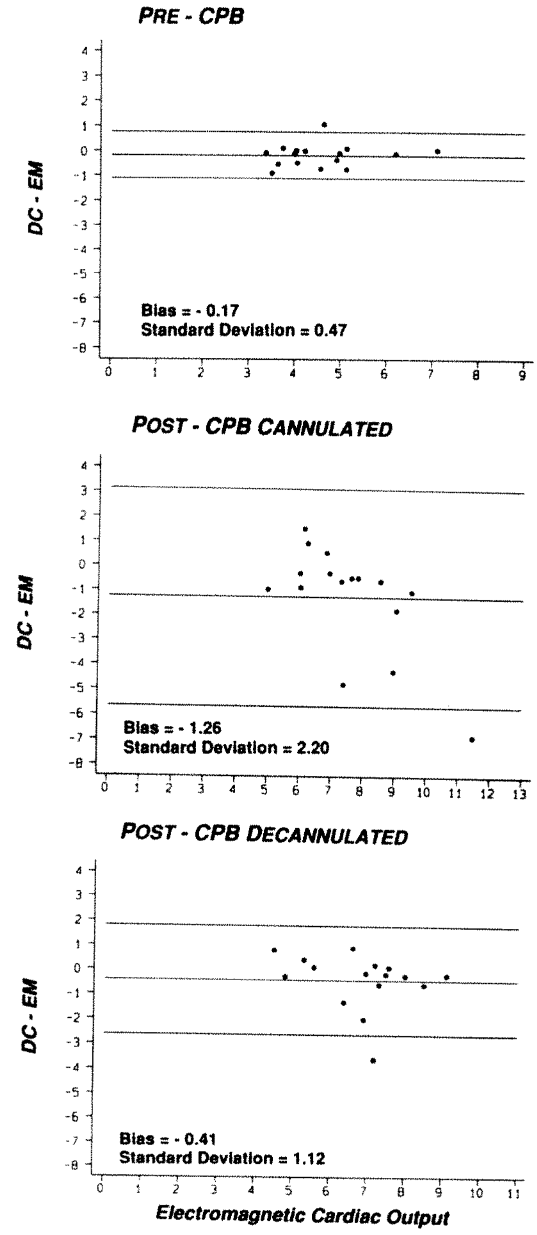


Fig 11. The Doppler cardiac output monitor (DOPCOM) − electromagnetic difference (DC − EM) plotted as a function of electromagnetic flow to determine bias and limits of agreement for measurements obtained at each of the three time points. Abbreviations are the same as in Figure 7.

Comment

When all data points are considered, TD and DOPCOM measurements of cardiac output show similar precision for predicting EM flow, although the DOPCOM appears to underestimate the EM value. However, both methods have distinct limitations. Thermodilution flow measurements, for example, varied widely (50% below to 80% above) from EM values in 2 of 3 patients with transesophageal echocardiographic evidence (color flow, pulsed Doppler, or both) of tricuspid regurgitation. This finding is not surprising in light of previous reports [6, 9, 10] that tricuspid regurgitation may alter TD estimation of cardiac output. Given recent evidence of an increased incidence of otherwise asymptomatic tricuspid regurgitation with age [11], the potential effect of valve dysfunction on TD cardiac output is worthy of consideration. It is interesting to note that in the 2 patients with markedly inaccurate TD measurements, DOPCOM measurements were far superior. When data from all 3 patients with tricuspid regurgitation were omitted, the TD and EM correlation improved to a level ($r = 0.92$) not dramatically different from that in the animal control ($r = 0.98$).

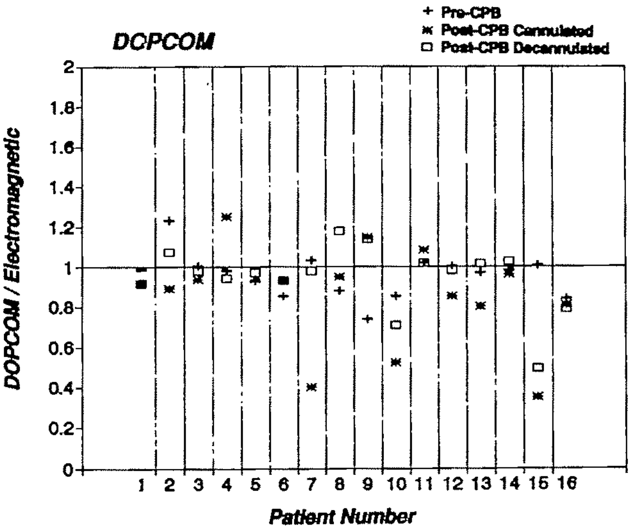


Fig 13. Relative accuracy of Doppler cardiac output monitor (DOPCOM) cardiac output measurements (DOPCOM/electromagnetic ratio) for each patient at each of the three time points. Abbreviations are the same as in Figure 7.

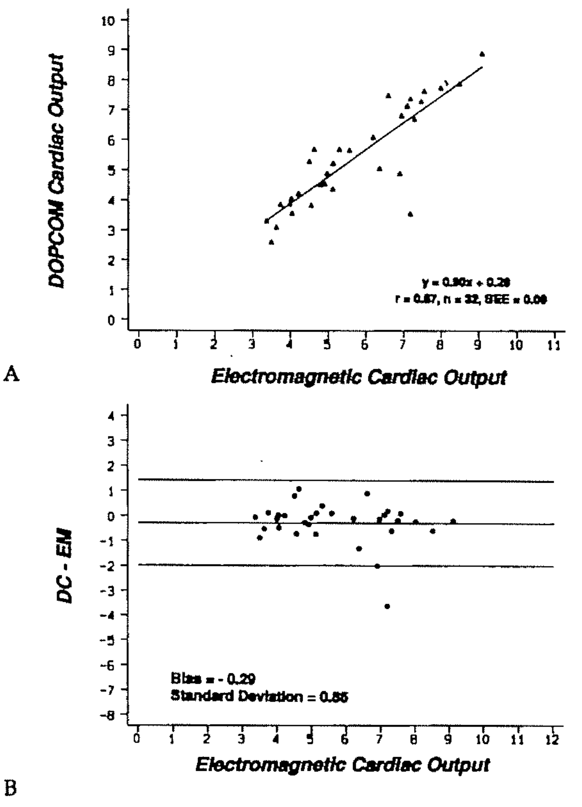


Fig 12. (A) Linear regression of Doppler cardiac output monitor (DOPCOM) cardiac output plotted as a function of aortic electromagnetic flow and (B) the DOPCOM − electromagnetic difference (DC − EM) for each measurement plotted as a function of electromagnetic flow to determine mean bias and limits of agreement (2 standard deviations from the mean bias). Data obtained immediately after cardiopulmonary bypass were omitted.

There were 3 patients in whom the DOPCOM did not work well after CPB with the aorta cannulated and volume intermittently infused. The Flocath is designed such that for the transducers to be in optimal position, the distal tip of the catheter must be positioned in the right PA. All attempts were made using transesophageal echocardiography to confirm initial appropriate placement, and the fact that DOPCOM measurements before CPB were more precise and less biased than TD values suggests optimal placement. However, catheter position was not reassessed after CPB. It is common practice at our institution to pull the PA catheter back 2 to 4 cm after the initiation of CPB and thus, it is quite possible that advancing the Flocath after CPB led to malpositioning in the left PA. The fact that all 3 patients with DOPCOM values markedly less than EM measurements after CPB had values close to EM values before CPB supports this possibility. In all probability, the malpositioned transducers could not accurately track the changes in PA diameter produced by volume infusion, thus leading to underestimation of cardiac output.

Given the similar precision of the DOPCOM and TD for predicting EM flow, the question remains whether the two methods are equally good or equally bad. Clearly the DOPCOM may be superior to TD in patients with known tricuspid regurgitation, but concerns about optimal positioning may undermine reliability after CPB. Alternatively, TD measurements are not subject to common catheter-positioning errors but are intermittent, influenced by respiration, and subject to operator error, and they may be unreliable in patients with occult tricuspid regurgitation. The DOPCOM system contains a position-alert function to notify the user that transducers may not be properly positioned for accurate diameter or velocity measurements, and under most circumstances, simple manipulation of the catheter is sufficient to correct the problem. However, this alert was not sounded in the 3 patients in this study whose DOPCOM values after CPB

Table 1. Statistical Comparison Between Thermodilution and Doppler Cardiac Output Monitor in Predicting Electromagnetic Measurement of Flow[a]

Variable	TD	DOPCOM	Median Difference
All Data			
Precision	0.53	0.51	0
	(0.20, 0.98)	(0.20, 0.870)	$p = 0.85$
Bias	−0.03	−0.28	0.10
	(−0.22, 0.39)	(−0.60, 0.01)	$p = 0.04$
Pre-CPB			
Precision	0.48	0.12	0.14
	(0.09, 1.59)	(0.05, 0.74)	$p = 0.04$
Bias	−0.16	−0.09	−0.17
	(−1.55, 0.23)	(−0.72, 0.11)	$p = 0.43$
Post-CPB cannulated			
Precision	0.41	0.90	−0.51
	(0.14, 107)	(0.46, 4.25)	$p = 0.65$
Bias	−0.03	−0.60	0.71
	(0.1, 2.0)	(−4.25, 0.55)	$p = 0.03$
Post-CPB decannulated			
Precision	0.83	0.34	0
	(0.10, 2.00)	(0.13, 1.31)	$p = 0.38$
Bias	0.33	−0.19	0.58
	(−0.18, 1.90)	(−1.31, 0.40)	$p = 0.03$

[a] Because the distribution of mean data was skewed by a few prominent outliers, analysis was performed on median values; 99% confidence limits are provided in parentheses for each median value to give an indication of expected sample-to-sample variation if the study were to be repeated under identical conditions.

Bias = the median amount (error) by which TD or the DOPCOM overestimates or underestimates electromagnetometry in liters per minute; DOPCOM = Doppler cardiac output monitor, Doppler pulmonary artery catheter system; Median difference = the median of the distribution of differences when all of the errors from DOPCOM are subtracted from TD errors (a sign-rank test was used to determine if the difference was different from 0; $p < 0.05$ was regarded as significant); Precision = the median absolute amount (error) by which TD or the DOPCOM misses electromagnetometry in liters per minute; Pre-CPB = before cardiopulmonary bypass; post-CPB cannulated = after CPB with the aortic perfusion cannula in place; post-CPB decannulated = after CPB with the aortic perfusion cannula removed; TD = thermodilution.

were widely different from EM measurements. Furthermore, it is undesirable to manipulate the catheter immediately after CPB, a particularly vulnerable period of the surgical procedure. It is not unreasonable, therefore, to manually feel for placement of the Flocath in the right PA before initiating mechanical ventilation and weaning from CPB, and to monitor continuous DOPCOM flow measurements along with intermittent TD cardiac output immediately after CPB.

The advantage of the DOPCOM system over TD appears to lie more in the beat-to-beat nature of the measurements than in absolute accuracy. Clearly it is desirable to display on the operating room monitor either a mean (updated every 4 or 20 seconds) or real-time pulsatile measurement of cardiac output. However, using the DOPCOM we have also measured other beat-to-beat variables such as PA compliance and blood acceleration (a relatively sensitive index of right ventricular contractility), right ventricular stroke work, peak ejection rate of change in right ventricular power, and continuous systemic vascular resistance. Thus it appears that the DOPCOM not only increases the convenience of cardiac output monitoring, but also may represent an important step in the evolution of methods to assess beat-to-beat ventricular function.

In summary, DOPCOM measurement of pulmonary arterial blood flow provides continuous monitoring of cardiac output, which, in general, is similar in precision to that of intermittent TD measurements. However, DOPCOM flow measurements may be more reliable than those of TD in patients with tricuspid regurgitation, and on-line processing of velocity, diameter, and flow measurements can potentially provide beat-to-beat information about cardiovascular function and reserve.

We thank Brent Pleimann for his help with data entry and figure preparation, Valerie Granger for typing the manuscript, and Dr Demetrios Lappas for his support and encouragement.

References

1. Segal J, Pearl RG, Ford AJ, Stern RA, Gehlbach SM. Instantaneous and continuous cardiac output obtained with a Doppler pulmonary artery catheter. J Am Coll Cardiol 1989; 13:1382–92.
2. Segal J, Nassi M, Ford AJ, Schuenmeyer TD. Instantaneous and continuous cardiac output in humans obtained with a Doppler pulmonary artery catheter. J Am Coll Cardiol 1990; 16:1398–1407.
3. Segal J, Gaudiani V, Nishimura T. Continuous determination of cardiac output using a flow-directed Doppler pulmonary artery catheter. J Cardiothorac Vasc Anesth 1991;5:309–15.
4. Ganz W, Donoso R, Marcus HS, Forrester JS, Swan HJC. A new technique for measurement of cardiac output by thermodilution in man. Am J Cardiol 1971;27:392–6.
5. Levett JM, Replogle RL. Thermodilution cardiac output: a critical analysis and review of the literature. J Surg Res 1979;27:392–404.
6. Heerdt PM, Pond CG, Blessios GA, Rosenbloom M. Inaccuracy of cardiac output by thermodilution during acute tricuspid regurgitation. Ann Thorac Surg 1992;53:706–8.
7. Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. Statistician 1983;32: 307–17.
8. Sheiner LB, Beal SL. Some suggestions for measuring predictive performance. J Pharmacokinet Biopharm 1981;9: 503–12.
9. Fischer AP, Benis AM, Jurado RA, Seely E, Teirstein P, Litwak RS. Analysis of error in measurement of cardiac output by simultaneous dye and thermal dilution in cardiothoracic surgical patients. Cardiovasc Res 1978;12:190–9.
10. Cigarroa RG, Lange RA, Williams RH, Bedotto JB, Hillis LD. Underestimation of cardiac output by thermodilution in patients with tricuspid regurgitation. Am J Med 1989;86: 417–20.
11. Klein AL, Burstow DJ, Tajik AJ, et al. Age-related prevalence of valvular regurgitation in normal subjects: a comprehensive color flow examination of 118 volunteers. J Am Soc Echo 1990;2:54–63.

Pulmonary Artery Sling

Ashwinikumar Pawade, FRCS, Marc R. de Leval, FRCS, Martin J. Elliott, FRCS, and Jaroslav Stark, FRCS

The Hospital for Sick Children, London, England

Eighteen patients who underwent surgical treatment of pulmonary artery sling at this institution since 1969 were reviewed. Four of them had associated tracheal stenoses produced by complete cartilaginous rings (stovepipe trachea). All patients underwent operation. The median age at operation was 180 days (range, 27 days to 54 months). In the 14 patients with isolated pulmonary sling, the operation consisted of division of left pulmonary artery and reimplantation into the main pulmonary artery anterior to the trachea. In the 4 patients with stovepipe trachea, the stenotic tracheal segment was resected on cardiopulmonary bypass and the left pulmonary artery was brought anterior to the trachea before the latter was reanastomosed to the main pulmonary artery. There were no early deaths. One patient died late. The pulmonary artery anastomosis was patent in all 14 patients investigated postoperatively. Three patients have residual tracheobronchial problems. One patient is mentally retarded and is institutionalized. All other patients are symptom-free and growing normally and have normal chest radiographs.

(Ann Thorac Surg 1992;54:967–70)

Pulmonary artery sling is a vascular abnormality wherein the left pulmonary artery arises from the right pulmonary artery and then traverses between the esophagus and the trachea toward the hilum of the left lung. This produces a sling around the distal trachea and the proximal main bronchi. Respiratory embarrassment can be caused by either mechanical compression, tracheomalacia, or long-segment tracheal stenosis due to associated complete cartilaginous rings of the trachea (the so-called O ring, napkin ring, or stovepipe trachea). The combination is sometimes called ring-sling syndrome [1].

Anomalous left pulmonary artery was first described in 1897 as a postmortem finding by Glaevecke and Doehle [2]. The term *pulmonary artery sling* was used by Contro and associates [3] in 1958 and has been popular ever since. In 1954 Potts and colleagues [4] described a repair consisting of division of the left pulmonary artery and reanastomosis of the two ends anterior to the trachea. The initial reports of surgical repair were dismal, with mortalities quoted from 38% to 50% [5, 6]. However, recent reports using microvascular surgery and heparin have been more encouraging [7–9].

We report our experience with 18 patients treated at our department since 1969.

Material and Methods

Patients

Since 1969, 18 patients (11 male and 7 female) underwent surgical treatment of pulmonary artery sling. Six patients have been previously reported [7, 9]. Four patients had associated tracheal strictures due to complete cartilaginous rings, the so-called stovepipe trachea. The age at which symptoms were first noticed ranged from 1 day to 4 months (median, 1 day). All the patients had wheeze, 11 patients had additional stridor, 7 patients had recurrent chest infections, and 3 patients fed poorly and failed to thrive. Eight patients were in acute respiratory failure and had to be ventilated at some stage before the operation; 6 of them were extubated successfully before operation. Predominant signs were stridor, tachypnea, and intercostal recession. The interval between the onset of symptoms and consultation for treatment ranged from 1 day to 19 months (median, 4 months).

Two patients treated were identical twins. Associated abnormalities were as follows: 4 patients had stovepipe trachea, 1 patient had a fibrous tracheal stricture, and 1 patient had a microtrachea. The patient with microtrachea died postoperatively, but the nature of the tracheal pathology was never determined. Two patients had agenesis of the right lung, 1 with dextrocardia and hemivertebra. One patient had subglottic stenosis, and 1 had Robert's syndrome, dextrocardia, left isomerism, and left superior vena cava.

Diagnosis was established predominantly by a barium swallow in 17 patients, although it was aided by an additional angiogram in 6 patients, magnetic resonance imaging in 2 patients, and computed tomographic scan in 1 patient. In 1 patient the barium failed to fill the esophagus adequately and the diagnosis was established by magnetic resonance imaging alone.

Chest roentgenogram was unremarkable in 6 patients; it showed a hyperinflated left lung in 3 patients, right upper lobe collapse in 5 patients, obstructive emphysema of the right upper lobe in 1 patient, a small right lung in 1 patient, and absent right lung in 2 patients.

A high-kV chest radiograph using special filters and magnification was found to be particularly useful. A long, narrow segment was suggestive of a stovepipe trachea,

---

Accepted for publication Aug 12, 1992.

Address reprint requests to Mr Stark, The Hospital for Sick Children, Great Ormond St, London, WC1N 3JH, England.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

whereas a discrete narrowing localized to the lower end of the trachea indicated simple mechanical compression by a pulmonary artery sling. Currently color-flow Doppler echocardiography can establish the diagnosis of pulmonary artery sling with great accuracy.

A preoperative bronchoscopy was performed in 11 patients. A stovepipe trachea was suspected when complete tracheal rings could be visualized and when the posterior wall of the trachea failed to move with the Venturi jet. This was observed in 4 patients. Currently we perform bronchoscopy before operation under the same anesthesia. The diagnosis of associated tracheal problems will determine the approach and also the need for the use of cardiopulmonary bypass.

Surgical Technique

The age at operation ranged from 27 days to 54 months (mean, 180 ± 35 days).

In patients with isolated pulmonary artery sling our preferred approach is through a left thoracotomy (10 patients). If cardiopulmonary bypass is needed, we use midline sternotomy. We elected to use cardiopulmonary bypass in 8 patients for the following reasons: tracheal resection (4 patients), agenesis of the right lung (2), origin of the left pulmonary artery too far to the right (1), and severe bradycardia caused by clamping of the left pulmonary artery (1).

In patients with isolated pulmonary artery sling, the surgical technique employed was as described by Dunn and associates [7]. A left thoracotomy was performed through the fourth intercostal space. The ligamentum arteriosum or persistent ductus arteriosus was divided, and the anomalous left pulmonary artery was identified as it emerged from underneath the aortic arch. The pulmonary artery was dissected as deep into the mediastinum as possible. After systemic heparinization (1 mg/kg body weight) the left pulmonary artery was occluded with snares at the primary branches. A vascular clamp was applied to the left pulmonary artery as deep as possible, and the artery was transected. The proximal stump was carefully oversewn with fine monofilament suture. Care was taken not to obstruct the trachea with the vascular clamp. The pericardium was opened posterior to the left phrenic nerve, and the main pulmonary artery was dissected. A partial occlusion clamp was used to isolate a portion of the main pulmonary artery, which was then incised. The left pulmonary artery was trimmed obliquely, brought through the pericardial incision, and sutured to the main pulmonary artery end-to-side, using a fine monofilament suture. A large anastomosis was constructed.

In patients with stovepipe trachea, the operation was performed through a median sternotomy. The trachea was mobilized well above and below the stricture. The ligamentum arteriosum was divided. Cardiopulmonary bypass was then established under mild hypothermia. The tracheal stricture was now excised, making sure that no complete rings were left behind. The left pulmonary artery was brought anteriorly through the gap in the trachea. Primary tracheal anastomosis was performed using interrupted sutures of 6-0 Prolene (Ethicon, Somerville, NJ). The tracheal tube was maintained high in the trachea. The anastomosis was tested to 40 cm H_2O for any evidence of an air leak and was then sealed with fibrin glue (Tisseel; Immuno, Austria). After rewarming, the patient was weaned from cardiopulmonary bypass.

Postoperative Care

Postoperatively, the patients were ventilated in the intensive therapy unit, ranging from 2 to 58 days (median, 4 days). The stay in the intensive therapy unit ranged from 2 days to 70 days (median, 6 days). The hospital stay ranged from 5 days to 90 days (median, 11 days).

Results

Mortality

There were no early deaths. One patient died late (5.5%). This patient had a pulmonary artery sling that was repaired through a left thoracotomy. A preoperative bronchoscopy showed that the trachea was considerably narrow. A diagnosis of microtrachea was made. The exact nature of the tracheal rings was not noted. The patient had respiratory difficulty on attempted extubation and subsequently underwent tracheal dilation and tracheostomy. She was readmitted 7 days after discharge in respiratory failure. She was ventilated, but air trapping and bilateral pneumothoraces developed and she died. A postmortem examination was not performed; therefore the exact pathological nature of the microtrachea remains unclear.

Morbidity

Two patients had to be reintubated after their first extubation because of atelectases. They were subsequently extubated successfully. Six patients had postoperative respiratory infections, which were treated with antibiotics and physiotherapy. One patient had a paralyzed left hemidiaphragm, which needed plication.

The follow-up is 100% complete and ranges from 2 months to 21 years (mean, 108 ± 35 months). Three patients have residual tracheobronchial problems manifest as wheeze and repeated respiratory infections. Two of them had undergone tracheal resections for stovepipe trachea. One of these has a lower tracheal stricture at the site of tracheal anastomosis, which stops short of the origins of the main bronchi. The other patient (mentally subnormal and institutionalized) has tracheomalacia at the carina. Both of them have to undergo regular bronchoscopy and dilation. The third patient with a residual problem had agenesis of the right lung associated with a pulmonary sling. He has malacia of the left upper lobe bronchus and requires frequent admissions to the intensive therapy unit for ventilation after atelectasis of the left upper lobe. All other patients have been reported to have normal growth and development.

Postoperative ventilation/perfusion scan was performed in 13 patients and showed a satisfactory perfusion on the repaired side. Patency of the left pulmonary artery was established in 1 additional patient by a computed tomographic scan, which was basically undertaken to assess the tracheal stricture. The 3 patients most recently operated on are awaiting their ventilation/perfusion scans.

Comment

Pulmonary artery sling is a condition that generally manifests in infancy and often with severe symptoms. Death from airway obstruction has been reported as early as 2 days after birth [3] and is common before the age of 6 months in untreated patients [10]. Very few cases of the asymptomatic form of pulmonary artery sling have been reported [11–13]. However, determination of the prevalence of the asymptomatic form of this disease is largely conjectural. In view of the seriousness of this condition and the fact that reports of surgical management have been encouraging, our policy has been to offer operation as soon as the diagnosis has been made.

Although all cases are grouped under a common category of pulmonary artery sling, we believe that there are two distinctly different entities. Group 1 includes patients with pulmonary artery sling. In this group patients can be operated on through a left thoracotomy and without cardiopulmonary bypass. The operation is relatively simple, and a complete cure can be achieved with a very low early mortality. Except for 1 patient who has bronchomalacia of the left upper lobe and agenesis of the right lung, no patient in this group has any residual problems. This indicates that in most of the patients the tracheal manifestations are due to a simple mechanical compression by the "sling" and therefore reversible once the compression is relieved.

Group 2 patients, on the other hand, have a coexisting tracheal stenosis due to complete tracheal rings and an absence of any substantial pars membranacea. This entity is also called a "stovepipe," "O ring," or "napkin ring" trachea. This was first described by Scheid in 1938 [14]. This association of pulmonary artery sling and stovepipe trachea was termed by Berdon and associates [1] as the *ring-sling* complex. Four of our patients (22%) were diagnosed to have this syndrome preoperatively. The patient with microtrachea who died probably had the same problem, although this was never diagnosed with certainty.

Associated stovepipe trachea may be suspected on plain chest radiograph, which may show normal findings or a symmetrical overaeration but no evidence of selective right-sided air trapping, emphysema, or atelectasis as in patients with isolated pulmonary artery sling [1]. This is to be expected as the problem is central in the trachea itself. High-kV filtered radiography using magnification [15] can often demonstrate the tracheal anomaly. A long-segment stricture is highly suggestive of a stovepipe trachea, whereas a small discrete stricture localized at the lower end of the trachea is probably from simple mechanical compression.

The final diagnosis rests on a bronchoscopy, which is best carried out just before definitive operation. Visualization of complete tracheal rings and absence of the normal movement of the posterior membranous wall of the trachea with the Venturi jet is diagnostic of stovepipe trachea.

As suggested by Grillo in the discussion of Dunn and associates [7] and by Jonas and associates [8], the primary approach in these cases is that of resection of the stricture and reanastomosis of the trachea behind the left pulmonary artery. The operation is carried out through a median sternotomy on cardiopulmonary bypass. Although the mortality for tracheal resection in the present series was nil, the morbidity has been considerable, with 2 patients continuing to have respiratory symptoms from residual tracheobronchial problems. It is therefore vital that a diagnosis of the ring-sling syndrome is made as soon as possible.

The mainstay of the diagnosis of pulmonary artery sling has been the barium esophagogram. A lateral view discloses an anterior indentation of the esophagus, a finding described with no other vascular lesion [16, 17].

We recommend that careful cardiological evaluation including echocardiography should be performed in all the patients to rule out associated cardiovascular lesions, which have been reported in 58% to 83% of patients [13]. Color-flow Doppler echocardiography may demonstrate the "sling" and establish the diagnosis. If there are any further doubts, angiocardiography or magnetic resonance imaging may be used.

The decision regarding the use of a median sternotomy and cardiopulmonary bypass depends on the presence or absence of tracheal stenosis. We prefer to use cardiopulmonary bypass during tracheal resections in infants, although such a practice is not universal [18, 19]. If there are associated cardiac lesions they can be repaired simultaneously in the same sitting [20].

Pulmonary artery sling could be treated surgically with a low mortality and morbidity. Patients with associated stovepipe trachea have poorer results when compared with those with pulmonary artery sling alone; early operation offers the only hope in this combination of lesions.

References

1. Berdon WE, Baker DM, Wung JT, et al. Complete cartilage-ring tracheal stenosis associated with anomalous left pulmonary artery: the ring-sling complex. Radiology 1984;152:57–64.
2. Glaevecke H, Doehle H. Uber cine seltene angeborene Anomalie der Pulmonalarterie. Munch Med Wochenschr 1897;44:950–1.
3. Contro S, Miller RA, White M, Potts WJ. Bronchial obstruction due to pulmonary artery abnormalities. I. Vascular ring. Circulation 1958;17:418–23.
4. Potts WJ, Holinger PM, Rosenblum AH. Anomalous left pulmonary artery causing obstruction to right main bronchus. JAMA 1954;155:1409–11.
5. Rheuban KS, Ayres N, Still G, Alford B. Pulmonary artery sling: a new diagnostic tool and clinical review. Paediatrics 1982;69:472–5.
6. Sade RM, Rosenthal A, Fellows K, Castanaeda A. Pulmonary artery sling. J Thorac Cardiovasc Surg 1975;69:333–46.
7. Dunn JM, Gordon I, Chrispin AR, et al. Early and late results of surgical correction of pulmonary artery sling. Ann Thorac Surg 1979;28:230–8.
8. Jonas RA, Spevak PJ, McGill T, Castanaeda AR. Pulmonary

artery sling: primary repair by tracheal resection in infancy. J Thorac Cardiovasc Surg 1989;97:548–50.
9. Westaby S, Dinwiddie R, Chrispin A, Stark J. Pulmonary artery sling in identical twins—report of two cases. Thorac Cardiovasc Surg 1984;32:182–3.
10. Gumbiner CH, Mullins CE, McNamara DG. Pulmonary artery sling. Am J Cardiol 1980;45:311–5.
11. Dupuis C, Vaksmann G, Pernot C, et al. Asymptomatic form of left pulmonary artery sling. Am J Cardiol 1988;61:177–81.
12. Steinberg I. Anomalous (non-constricting) left pulmonary artery. Circulation 1964;29:897–900.
13. Philip T, Sumerling MD, Fleming J, Grainger MG. Aberrant left pulmonary artery. Clin Radiol 1972;23:153–9.
14. Scheid P. Missbilding des Traachealskelettes und der linken Arteria pulmonalis mit Erstickungstod bei 7 monate alt Kind. Frank Zeitschr Pathol 1938;52:114–6.
15. Joseph PM, Walter EB, Baker DH, et al. Upper airway obstruction in infants and small children. Paediatric Radiology 1976;121:143–8.
16. Singleton EB, Wagner ML. Radiologic atlas of pulmonary abnormalities in children. Philadelphia: Saunders, 1971:85.
17. Capitano MA, Ramos R, Kirkpatrick JA. Pulmonary sling, roentgen observations. Am J Radiol 1971;112:28–34.
18. Nakayama DK, Harrison MR, de Lorimier AA, et al. Reconstructive surgery for obstructing lesions of the intrathoracic trachea in infants and small children. J Paediatr Surg 1982; 84:200–3.
19. Mattingley WT Jr, Belin RP, Todd EP. Surgical repair of congenital tracheal stenosis in an infant. J Thorac Cardiovasc Surg 1981;81:738–40.
20. Yamaguchi M, Oshima Y, Hosokawa Y, et al. Concomitant repair of congenital tracheal stenosis and complex cardiac anomaly in small children. J Thorac Cardiovasc Surg 1990; 100:181–7.

Pulmonary Artery Sling With Tracheal Stenosis: Primary One-Stage Repair in Infancy

Gerhard Ziemer, MD, Markus Heinemann, MD, Renate Kaulitz, MD,
Joachim Freihorst, MD, Jürgen Seidenberg, MD, and Martin Wilken, MD

Surgical Center, Division of Thoracic and Cardiovascular Surgery I, Children's Hospital, Divisions of Pediatric Cardiology and Pulmonology, Hannover Medical School, Hannover, Germany

Pulmonary artery sling is often associated with tracheal stenosis. In many cases repair of the vascular anomaly alone does not relieve dyspnea. Primary one-stage repair with long segment tracheal resection (2.4 cm) and relocation of the left pulmonary artery using cardiopulmonary bypass and deep hypothermic circulatory arrest is described in a 6.5-month-old girl weighing 6.5 kg. This technique resulted in normal ventilation and pulmonary flow distribution.

(Ann Thorac Surg 1992;54:971–3)

Pulmonary artery sling is defined as an abnormal origin of the left pulmonary artery, originating distally from the right vessel, and reaching the left lung by passing between trachea and esophagus [1, 2]. This, in combination with the ligamentum arteriosum between the left pulmonary artery and aorta, forms a vascular ring which may remain asymptomatic. About 90% of the patients become symptomatic with respiratory distress; the average age at onset of symptoms is 2 months [3]. In 50% of the patients, this malformation is associated with other congenital heart defects; 55% to 60% show morphological stenoses of the distal trachea or right main bronchus as well as left main bronchial stenosis [2]. In some of the latter patients, the pars membranacea is absent, the cartilages forming complete rings resulting in a hypoplastic airway and severe dyspnea [4]. This cannot be relieved by repair of the vascular anomaly alone.

A 6.5-month-old girl weighing 6.5 kg had been intubated and intermittently ventilated for 4 months because of "extreme obstructive airway disease." She was referred to our hospital for evaluation when the respiratory situation had become critical under ventilation.

Bronchoscopy revealed a blindly ending anomalous right upper lobe bronchus ("pig bronchus") and subtotal stenosis of the distal trachea. On bronchography there was severe narrowing of the distal third of the trachea, starting at the origin of the anomalous bronchus (Fig 1). Echocardiography and cardiac catheterization showed a hypoplastic left pulmonary artery coming off the right vessel, as well as a patent foramen ovale and a small perimembranous ventricular septal defect.

The operation was performed through a median sternotomy on cardiopulmonary bypass. The restrictive ligamentum arteriosum was divided. The hypoplastic left pulmonary artery was dissected free and divided at its origin from the right pulmonary artery. Circulatory arrest was established when deep hypothermia (rectal temperature, 20°C) was reached. The patent foramen ovale was closed by direct suture. Because of its small size and fibrotic rims, the ventricular septal defect was also closed directly through the right atrium with several interrupted U-stitches buttressed with autologous pericardium. Then the trachea was dissected free anteriorly and posteriorly, care being taken to spare the lateral connective tissue bearing the blood supply. Both main bronchi were partially dissected. Then the stenotic segment was resected in three steps. The specimen showed complete cartilaginous rings extending over a length of 2.4 cm, about one third of the total length of the trachea. The segment resected included the tracheal origin of the blindly ending anomalous right upper lobe bronchus (Fig 2).

Both main bronchi were incised longitudinally to match the circumference of the proximal trachea (Figs 3, 4). An end-to-end anastomosis of the trachea with the carina was performed, using a 5-0 polydioxanone (PDS, Ethicon, Somerville, NJ) continuous suture for the back wall and interrupted sutures for the anterior wall. The anastomosis was sealed externally with fibrin glue (Immuno AG, Vienna, Austria) mixed with neomycin and bacitracin [5]. Then the hypoplastic left pulmonary artery was anastomosed to the main pulmonary artery dorsolaterally, using a continuous 6-0 polydioxanone suture (PDS, Ethicon). Its lumen was found to be only half that of the right pulmonary artery. Weaning from bypass was without problems (total cardiopulmonary bypass time, 136 minutes; aortic cross-clamp time, 51 minutes; circulatory arrest, 46 minutes). To prevent tension at the anastomosis, a plaster cast was applied around the girl's head, holding it in ventroflexion for 2 weeks.

Early postoperatively some glutinous mucus had to be removed from the airways bronchoscopically. The child was extubated on the 6th postoperative day without stridor. Apart from some initial bronchospasm, further recovery was uneventful. A final bronchoscopy 5 weeks

---

Accepted for publication Dec 6, 1991.

Address reprint requests to Dr Ziemer, Surgical Center, Division of Thoracic and Cardiovascular Surgery, Hannover Medical School, Konstanty-Gutschow-Str 8, D-3000 Hannover 61, Germany.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

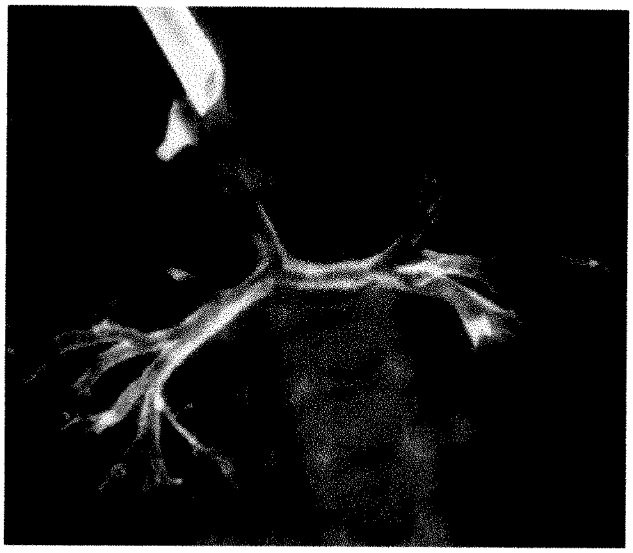


Fig 1. Preoperative bronchography: In anteroposterior view the contrast-filled, blindly ending "pig bronchus" is clearly visualized. The stenotic segment starts at the origin of this anomalous bronchus and connects to the carina.

postoperatively showed a normal tracheal lumen with the anastomosis barely visible (Fig 5). In a ventilation/perfusion lung scan, ventilation was equal on both sides (48% left, 52% right). Perfusion was slightly lower on the left side (40% left, 60% right). This is explained by the hypoplasia of the left pulmonary artery. Lung function tests were normal. Twenty-six months postoperatively the girl continues to be asymptomatic and she shows normal physical and psychological development without any signs of respiratory or cardiac impairment.

Comment

A malformation of the pulmonary arteries being the cause of tracheal obstruction was first described by Glaevecke and Doehle [6]. In 1954, Potts and associates [7] reported the first successful relocation of the left pulmonary artery in pulmonary artery sling through a right thoracotomy. This became the standard operation for this malformation and was usually performed through a left thoracotomy. Results with this approach were equivocal. Despite reports describing a low initial risk [8], several authors reported residual or recurrent tracheal stenoses leading to considerable mortality [1, 2]. Thus, several techniques were applied to relieve the tension on the trachea by keeping it apart from the relocated pulmonary artery: Dunn and co-workers [8] emphasized the importance of division of the ligamentum arteriosum, Campbell and associates [9] advised relocation of the left pulmonary artery combined with aortopexy through a sternotomy, and Conti and Lobe [10] recommended tracheopexy.

In cases of morphological tracheal stenosis caused by cartilaginous rings, these methods will not bring long-

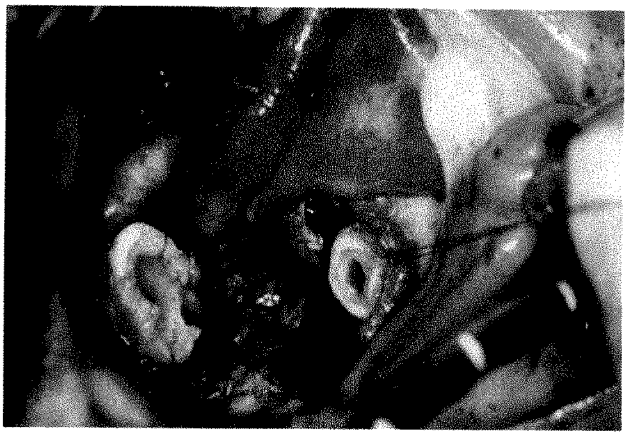


Fig 3. Tracheal situs after first resection: The two central segments of Figure 2 are resected. On the left the cranial end, resected just proximal to the origin of the pig bronchus, has a normal diameter. On the right the distally resected end, just proximal to the carina, is still severely stenotic.

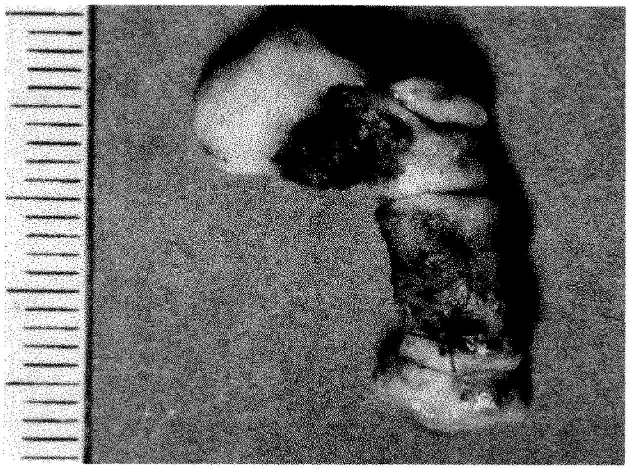


Fig 2. Resection specimen: Resected in four segments; the reconstruction resembles the tracheal anatomy as outlined in the preoperative bronchography. (Length, 2.4 cm.)

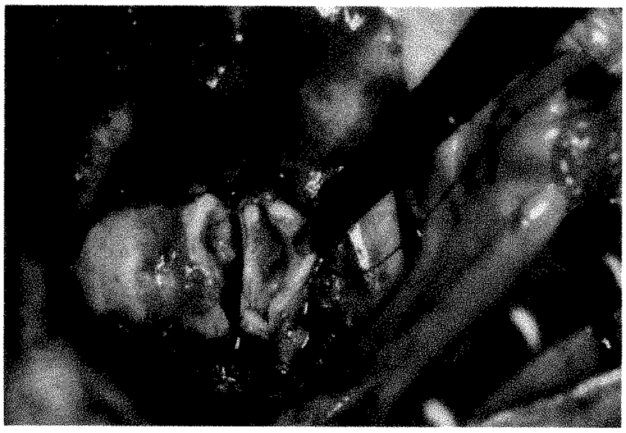


Fig 4. Final tracheal resection situs before anastomosis: Two more segments are resected, most importantly the distal one, opening up the carina. To match the circumference of the proximal trachea, small longitudinal incions into both main bronchi were necessary. Approximation of the cut ends was possible without serious tension.

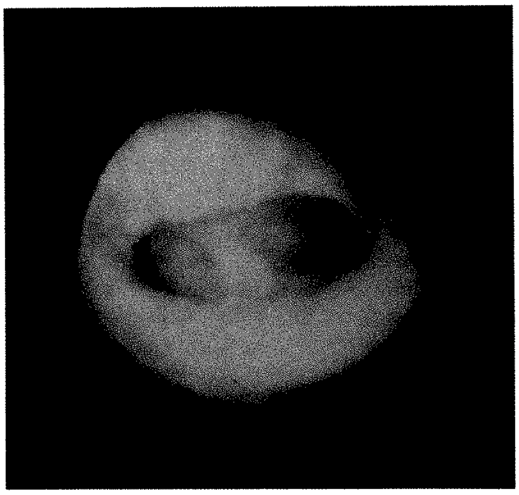


Fig 5. Postoperative tracheoscopy: Five weeks postoperatively the distal trachea looks normal without any suture material being visible.

standing relief because they do not correct the malformation [4, 11]. Jonas and colleagues [12] therefore used cardiopulmonary bypass to resect the stenotic trachea in combination with a left pulmonary arteriopexy. In 1987, Hickey and Wood [13] reported the first total one-stage repair of pulmonary artery sling and tracheal stenosis. They resected the stenotic tracheal segment and relocated the left pulmonary artery through a sternotomy, using cardiopulmonary bypass, in a 4.5-year-old boy.

Because of possible associated morphological abnormalities of the tracheobronchial system, preoperative evaluation in children with pulmonary artery sling must include bronchoscopy or bronchography, as well as barium swallow, two-dimensional echocardiography, and cardiac catheterization [11–13]. If the condition is confirmed, we believe that the logical, corrective procedure for this combined disease is correcting the two malformations involved, namely, tracheal stenosis and anomalous origin/course of the left pulmonary artery. In this aspect, our report is very similar to that of Hickey and Woods [13]; however, we had to resect a much longer segment (2.4 cm versus 1.0 cm) in a much younger patient (6 months versus 4.5 years). Another difference is the use of deep hypothermic circulatory arrest in our patient. Deep hypothermic circulatory arrest is our routine procedure in infant intracardiac operations—ventricular septal defect closure in this case—and once employed it facilitated the additional tracheal resection. We would not employ deep hypothermic circulatory arrest for isolated tracheal resection.

Although it is known that bronchus suis—pig bronchus—can appear in pulmonary artery sling [11], our case is unusual in that this abnormal bronchus is blindly ending. As seen in the preoperative bronchogram (see Fig 1), there is a normal origin of a right upper lobe bronchus giving evidence for a normal right upper lobe bronchial anatomy in spite of the pig bronchus present.

Only tracheal resection can bring relief of the respiratory tract obstruction, and therefore it probably is the crucial part of the operation [12–14]. The left pulmonary artery is often hypoplastic. To bring it into a position free of additional kinking, precise anatomical relocation into the main pulmonary artery seems mandatory to avoid the poor patency rates of the past, when it was used without concomitant tracheal resection [8]. Our patient has excellent perfusion of the left lung after precise anatomical relocation of the left pulmonary artery.

In their report on 2 cases Jonas and associates [12] also focus on tracheal resection. After tracheal resection the left pulmonary artery was brought anteriorly through the gap in the trachea before tracheal reanastomosis was performed. Jonas and associates stated that if both tracheal resection and pulmonary artery reimplantation are performed, one of these two procedures appears to be redundant. During our procedure we believed anteropexy alone would have resulted in left pulmonary artery stenosis due to posterior impression by the reconstructed trachea. In their article, Jonas and associates did not present any data on patency of the left pulmonary artery in their patient with two lungs, and they did not rule out stenosis or kinking of the left pulmonary artery in the patient with absent right lung.

Our case shows that even in long hypoplastic tracheal segments, complete primary one-stage repair of symptomatic pulmonary artery sling—tracheal resection and left pulmonary artery reimplantation—can be performed in infancy, leading to pulmonary flow distribution and ventilation within the normal range.

References

1. Koopot R, Nikaidoh H, Idriss FS. Surgical management of anomalous left pulmonary artery causing tracheobronchial obstruction. Pulmonary artery sling. J Thorac Cardiovasc Surg 1975;69:239–46.
2. Sade RM, Rosenthal A, Fellows K, Castaneda AR. Pulmonary artery sling. J Thorac Cardiovasc Surg 1975;69:333–46.
3. Grover FL, Norton JB, Webb GE, Trinkle JK. Pulmonary sling. Case report and collective review. J Thorac Cardiovasc Surg 1975;69:295–300.
4. Cohen SR, Landing BH. Tracheostenosis and bronchial abnormalities associated with pulmonary artery sling. Ann Otol 1976;85:582–90.
5. Haverich A, Frimpong-Boateng K, Wahlers TW, Schaefers J. Pericardial flap plasty for protection of the tracheal anastomosis in heart-lung transplantation. J Cardiac Surg 1989;4:136–9.
6. Glaevecke H, Doehle W. Ueber eine seltene angeborene Anomalie der Pulmonalarterie. Muench Med Wochenschr 1897;44:950–3.
7. Potts WJ, Holinger PH, Rosenblum AH. Anomalous left pulmonary artery causing obstruction to right main bronchus. JAMA 1954;155:1409–11.
8. Dunn JM, Gordon I, Chrispin AR, de Leval MR, Stark J. Early and late results of surgical correction of pulmonary artery sling. Ann Thorac Surg 1979;28:230–8.
9. Campbell DN, Lilly JR, Heiser JC, Clarke DR. The surgery of pulmonary artery "sling." J Pediatr Surg 1983;18:855–6.
10. Conti VR, Lobe TE. Vascular sling with tracheomalacia: surgical management. Ann Thorac Surg 1989;47:310–1.
11. Castaneda AR. Pulmonary artery sling. Ann Thorac Surg 1979;28:210–1.
12. Jonas RA, Spevak PJ, McGill T, Castaneda AR. Pulmonary artery sling: primary repair by tracheal resection in infancy. J Thorac Cardiovasc Surg 1989;97:548–50.
13. Hickey MStJ, Wood AE. Pulmonary artery sling with tracheal stenosis: one-stage repair. Ann Thorac Surg 1987;44:416–7.
14. Longaker MT, Harrison MR, Adzick NS. Testing the limits of neonatal tracheal resection. J Pediatr Surg 1990;25:790–2.

Surgically Created Wolff-Parkinson-White Syndrome After Fontan Operation

Anees J. Razzouk, MD, Robert Gow, MB, BS, John Finley, MD, David Murphy, MD, and William G. Williams, MD

Divisions of Cardiology and Cardiovascular Surgery, Hospital for Sick Children, Toronto, and the Izaak Walton Killam Children's Hospital, Halifax, Canada

The Wolff-Parkinson-White syndrome is caused by a congenital accessory connection between the atrium and ventricle. We describe a case of symptomatic Wolff-Parkinson-White syndrome that arose after a Björk modification of the Fontan operation. Invasive electrophysiologic and intraoperative mapping indicated that the surgically created atrioventricular connection was functioning as an accessory pathway. Surgical dissection and cryoablation abolished the symptoms and the preexcitation.

(Ann Thorac Surg 1992;54:974–7)

The term *Wolff-Parkinson-White* (WPW) *syndrome* refers to the occurrence of supraventricular tachycardias in the presence of typical electrocardiographic findings. This syndrome may complicate a variety of acquired and congenital heart defects [1, 2]. Wolferth and Wood [3, 4] first hypothesized that the anatomic substrate was due to abnormal muscular connections between the atrium and ventricle. Proof for this concept was offered by Sealy and colleagues [5] after successful surgical division of an accessory pathway.

This case report illustrates the de novo development of the WPW syndrome subsequent to a Fontan operation in which a Björk-type atrioventricular (AV) connection was constructed [6]. Preoperative and intraoperative electrophysiologic mapping supports this being a surgically created preexcitation syndrome.

The patient was born on April 4, 1972, and a diagnosis of tricuspid atresia and normally related great vessels was made in the neonatal period. Initial palliation at 18 months of age was by a cavopulmonary connection (Glenn anastomosis). In January 1980 she underwent enlargement of the ventricular septal defect because of increasing cyanosis. When the patient was 12 years of age a modified Fontan procedure with a Björk-type connection was performed. No electrocardiogram before the Fontan operation showed any evidence of preexcitation (Fig 1A). Three years later she reported episodes of palpitations at rest and with exercise. There were no complaints of chest pain, syncope, or orthopnea, and she was not cyanotic. Moderately severe left AV valve regurgitation was noted on clinical examination. Echocardiography demonstrated an isolated cleft in the anterior leaflet of the mitral valve. Electrocardiogram demonstrated a preexcitation pattern consistent with the WPW syndrome (Fig 1B). Pharmacologic management (metoprolol, sotalol, digoxin) was not successful in controlling her symptoms. The patient was referred for electrophysiologic investigation and possible operation to divide the accessory pathway and repair the mitral valve.

Electrophysiologic study was performed under sedation with meperidine hydrochloride (Demerol; Winthrop Pharmaceuticals, New York, NY) and promethazine after all antiarrhythmic drugs had been withdrawn for 48 hours. At the time of study the electrocardiogram did not show evidence of preexcitation. Quadripolar catheters were placed in the high right atrium, in the coronary sinus, and in the small right ventricle through the Björk connection. Ventricular pacing protocols demonstrated nondecremental retrograde conduction with the earliest retrograde activation at the right free wall. Supraventricular tachycardia was induced by placing premature beats into paced ventricular rhythm. The supraventricular tachycardia cycle length was 344 ms, and catheter mapping revealed that earliest atrial activation occurred at the base of the right atrial appendage near the Björk connection (Fig 2). Posterior and lateral right atrium were activated late. Atrial activation was advanced by a premature ventricular beat placed at a time when the His bundle would be refractory. The findings were interpreted as indicating the presence of a single right-sided accessory pathway at the base of the right atrial appendage near the Björk connection, which had become manifest in the years after the Fontan operation.

In January 1990, the patient underwent repair of the mitral valve cleft and surgical division of the accessory pathway. Preexcitation was not evident at any time during the operative study. An intraoperative electrophysiologic map during ventricular pacing and supraventricular tachycardia revealed inappropriate early activation on either side of the previously constructed Björk connection where the right atrial muscle had been used as a flap and sewn to the adjacent incision in the right ventricular outflow tract (Fig 3). With the patient on normothermic

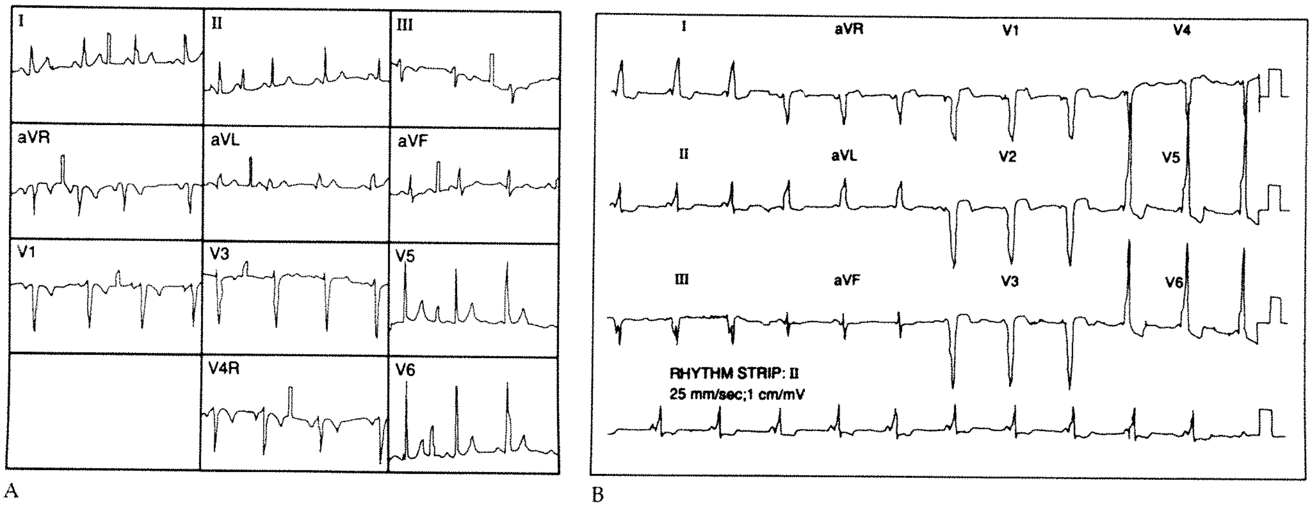
---

Accepted for publication Feb 10, 1992.

Address reprint requests to Dr Williams, No. 1525, 555 University Ave, Toronto, Ont, M5G 1X8, Canada.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00



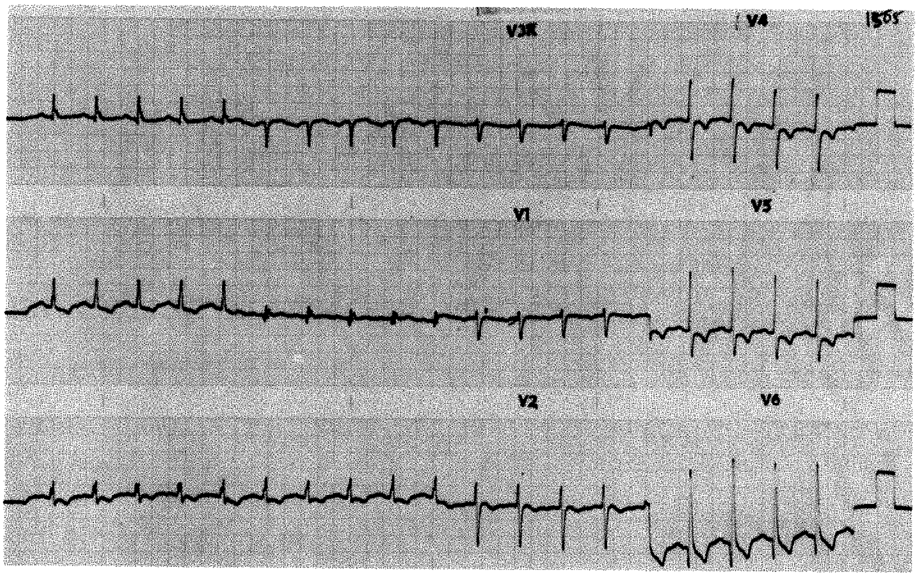


Fig 1. (A) Twelve-lead electrocardiogram taken before Fontan operation shows a normal PR interval and no preexcitation. (B) Electrocardiogram taken 1 year after the Fontan operation shows evidence of preexcitation with a short PR interval and delta waves. The pattern is consistent with a right-sided accessory pathway. (C) Electrocardiogram before hospital discharge after successful division of the atrioventricular connection.

cardiopulmonary bypass, endocardial mapping was carried out through an opening made in the pericardial tunnel that was part of the atrioventricular connection. These findings suggested that the accessory pathway was within the AV flap (*B3* in Fig 3). The junction between the atrium and ventricle was exposed, and repeat mapping confirmed early activation in the atrial flap itself (*B2* and *B3*, Fig 3). The posterior wall of the atrium where the atrial flap had been rotated onto the ventricle was divided. This maneuver broke the tachycardia, and subsequent mapping demonstrated no retrograde conduction from the ventricle to the body of the atrium, although there was persistent retrograde conduction from the ventricle into the distal narrow, isolated segment of atrium attached to the ventriculotomy. Cryolesions were placed along the AV junction in this area. Although the patient had a difficult postoperative course, which was complicated by mediastinitis, she is now fully recovered and remains in sinus rhythm free of supraventricular tachycardia on no antiarrhythmic medication (Fig 1C).

Comment

It is postulated that accessory atrioventricular conduction pathways result from incomplete separation of fetal atria and ventricles during development of the fibrous annulus of the heart [7]. The region of the annulus fibrosus where the atria and ventricles are not in continuity during fetal development lies between the right and left fibrous trigones, explaining why abnormal pathways may occur at any point around the annulus of either AV valve, except along the region of mitral-aortic continuity [8]. The majority of patients with preexcitation have morphologically normal hearts. Ebstein's anomaly of the tricuspid valve is the most common form of congenital heart disease in

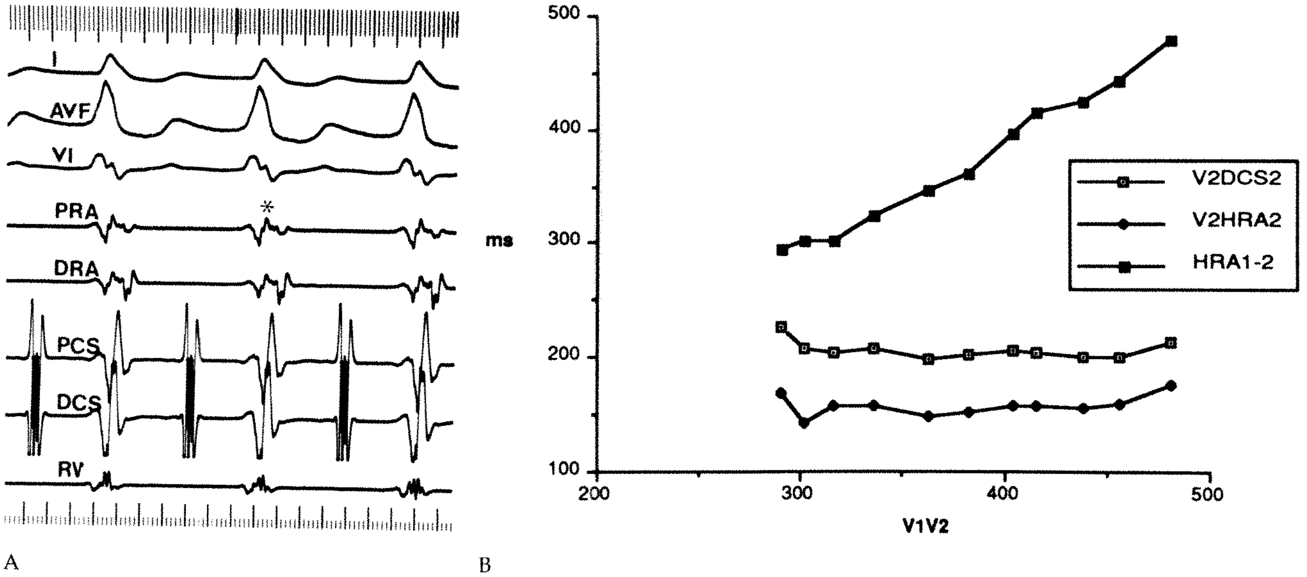


*Fig 2. (A) Surface electrocardiographic leads 1, aVF, and V_1, together with proximal and distal right atrial (*PRA, DRA*), proximal and distal coronary sinus (*PCS, DCS*), and right ventricular (*RV*) electrograms. Shown is supraventricular tachycardia with a cycle length of 344 ms. Earliest retrograde atrial activation occurs in the right atrial catheter, which is positioned anteromedially near the base of the Björk connection (*). (B) Graph of premature ventricular complexes (*V2*) into paced ventricular rhythm (*V1*). Retrograde atrial activation times were assessed in the high right atrium (*HRA*) and distal coronary sinus (*DCS*) in response to V2, and are represented by* V2HRA2 *and* V2DCS2. *Nondecremental conduction is shown, which is consistent with retrograde conduction over a muscular atrioventricular connection.*

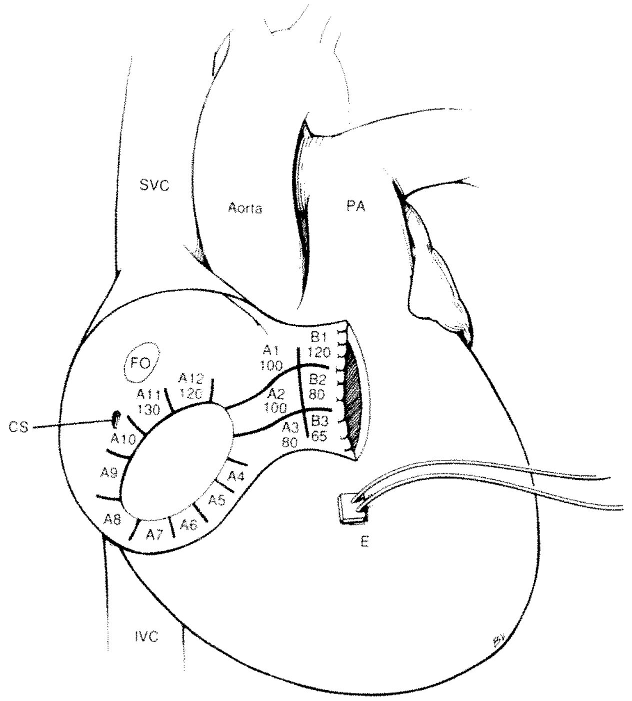


*Fig 3. Map of retrograde activation times within the atrioventricular flap taken during supraventricular tachycardia, from the ventricular reference electrogram (*E*) to the local atrial electrogram. The earliest activation was 65 ms at site* B3. *Activation from an accessory pathway would be expected to occur in row* A *before row* B. *(*CS *= coronary sinus;* FO *= foramen ovale;* IVC *= inferior vena cava;* PA *= pulmonary artery;* SVC *= superior vena cava.)*

patients with preexcitation, although many associations have been documented [1, 2].

This case report describes an accessory conduction pathway that was localized to the site of anastomosis between a right atrial flap and ventriculotomy subsequent to performance of a Björk-type modified Fontan operation. It is possible that an accessory pathway was always present and became manifest after the initial operation, as was suspected after the catheter mapping. The preoperative mapping was consistent with a right anterior free wall pathway, and the nondecremental properties indicate it consisted of working myocardium. The intracardiac mapping localized the retrograde pathway to the flap of atrial appendage that had been turned down and sutured onto the right ventricle. We believe that the evidence is strongly in favor of the functional accessory pathway having been "created" at the Fontan operation 5 years earlier. If the findings represented a preexisting accessory pathway, the retrograde activation pattern would most probably have proceeded from A3 to B3 as the impulse crossed the area of the rudimentary AV ring. Division of the atrial flap alleviated the arrhythmia; however, impulses were still able to enter the distal portion of the connection.

Experimental attempts to create AV conduction in animals with induced AV block by sewing a flap of atrial muscle to the adjacent ventricular epicardium frequently resulted in conduction through the atrial connection, which was accompanied by evidence of short PR intervals, and slurred QRS complexes (Yao J, personal communication).

Twenty-one children have undergone a Björk modification of the Fontan operation for tricuspid atresia at our institutions. None of these patients had evidence of WPW syndrome before operation; however, shortening of the PR interval, loss of initial Q waves, and delta waves have developed in 3 children during follow-up. Electrophysiologic confirmation has only been obtained in the patient who is the subject of this case report. Comparison with children with tricuspid atresia undergoing an atriopulmonary connection is revealing. Of 43 patients with long-term follow-up (median, 2.8 years), no patient had new evidence of WPW in the postoperative period. We believe this is further evidence supporting the contention that the surgically created AV connection was the source of preexcitation in this patient.

An important concept that is of interest in WPW operations is illustrated by these observations. The possibility is raised that recurrence may develop in patients in whom a surgical dissection has been performed for accessory conduction pathways by virtue of recovery of conduction across the divided and resutured atrial wall. Perhaps additional modalities (cryothermy, electrocautery) should supplement the surgical dissections for accessory pathways.

Based on our limited experience and on laboratory observations, we believe that accessory pathways are not always congenital, but may develop when atrial muscle is anastomosed to ventricular muscle.

References

1. Wolff L, Parkinson J, White PD. Bundle-branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. Am Heart J 1930;5:685–704.
2. Porter CJ, Holmes DR Jr. Preexcitation syndromes associated with congenital heart disease. In: Benditt DG, Benson DW, eds. Cardiac preexcitation syndromes: origins, evaluation and treatment. Boston: Martinus Nijhoff, 1986:289–301.
3. Wolferth CC, Wood FC. The mechanism of production of short PR intervals and prolonged QRS complexes in patients with presumably undamaged hearts: hypothesis of an accessory pathway of auriculo-ventricular connection (bundle of Kent). Am Heart J 1933;8:297–311.
4. Wood FC, Wolferth CC, Geckeler GD. Histologic demonstration of accessory muscular connections between auricle and ventricle in a case of short PR interval and prolonged QRS complex. Am Heart J 1943;25:454–62.
5. Sealy WC, Hattler BG Jr, Blumenschein SD, Cobb FR. Surgical treatment of Wolff-Parkinson-White syndrome. Ann Thorac Surg 1969;8:1–11.
6. Björk VO, Olin CL, Bjarke BB, Thoren CA. Right atrial–right ventricular anastomosis for correction of tricuspid atresia. J Thorac Cardiovasc Surg 1979;77:452–8.
7. Lunel AAV. Significance of annulus fibrosus of heart in relation to AV conduction and ventricular activation in cases of Wolff-Parkinson-White syndrome. Br Heart J 1972;34: 1263–71.
8. Cox JL. The surgical management of cardiac arrhythmias. In: Sabiston DC, Spencer FC, eds. Surgery of the chest. Philadelphia: Saunders, 1990:1861–990.

True Aneurysm of the Saphenous Vein Graft Stump Associated With CABG in a Cardiac Transplant Patient

Robert T. Baldwin, MD, Tomas Klima, MD, O. H. Frazier, MD, James Lonquist, MD, and Branislav Radovancevic, MD

Sections of Cardiovascular Surgery and Pathology, Texas Heart Institute, Houston, Texas

Aneurysm of a saphenous vein graft after coronary artery bypass requires surgical resection because of its potential for rupture. This report describes a case of aneurysm formation in a 55-year-old man who underwent coronary artery bypass operation in 1977 and orthotopic heart transplantation 7 years later. A proximal vein graft remnant that had been ligated at the time of transplantation developed into a 5-cm aneurysm. In patients who have undergone previous coronary artery bypass operation, we recommend that the entire vein graft stump be excised and oversewn at the aortosaphenous anastomosis at the time of transplantation.

(*Ann Thorac Surg 1992;54:978–9*)

The first true aneurysm of a saphenous vein graft was reported in 1972 and involved a patient who had undergone a vein graft repair of the carotid artery [1]. Aneurysm of an aortocoronary vein graft was first reported in 1975. In this patient, a well-circumscribed lesion adjacent to the aortic knob was noted on a routine chest radiograph 1 year after coronary artery bypass and was subsequently found to be a true aneurysm of the saphenous vein [2]. Four other cases have been reported [3–7] since this time; in 2 of those cases, hemorrhagic shock resulted from aneurysmal rupture [6, 7]. Because of this risk, vein graft aneurysms should be surgically excised to prevent death from exsanguination.

This report presents an unusual case of an aneurysm of the vein graft stump that occurred 7 years after heart transplantation. A complete excision of the vein at the time of heart transplantation or repeat coronary bypass may eliminate the possibility of the formation of such a life-threatening aneurysm.

A 55-year-old man had shortness of breath and symptoms of congestive heart failure 7 years after undergoing an orthotopic heart transplantation. At age 40 years, he had an inferior wall myocardial infarction and subsequently underwent aortocoronary bypass grafting of the right coronary, left anterior descending, first diagonal, and first and second obtuse marginal coronary arteries with an atraumatic saphenous vein harvest technique. He had symptoms of congestive heart failure at age 48 years, and results of cardiac catheterization showed poor ventricular function with 3 of 5 vein grafts occluded. He had orthotopic heart transplantation with ligation of the proximal vein graft segments at the time of recipient cardiectomy. He required moderate antihypertensive therapy and an immunosuppressive regimen consisting of cyclosporine, prednisone, and azathioprine for the next 7 years. Eventually dyspnea developed along with graft atherosclerosis in proximal coronary arteries. When the patient was 52 years old, percutaneous transluminal coronary angioplasty was performed on his left anterior descending coronary artery stenosis.

Upon readmission for his dyspnea, a chest radiograph showed a 5-cm anterior mediastinal mass that was not present in a radiograph taken 6 months earlier. Computed tomography and magnetic resonance imaging scans (Fig 1) confirmed the presence of the chest mass. Cardiac catheterization showed atherosclerosis in proximal coronary arteries but failed to show the cause of the mass.

The patient underwent mediastinal exploration and aortocoronary bypass to the left anterior descending and first obtuse marginal coronary arteries. A large clot-filled aneurysm of the saphenous vein graft remnant was excised and a Dacron graft patch angioplasty of the ascending aorta was performed. From within the aorta, the anastomotic suture line of the saphenous vein aneurysm was noted to be intact. The patient's postoperative course was complicated by preexisting pulmonary and renal insufficiency. He died of sepsis and multiorgan failure 22 days after operation.

Histopathologic examination of the mass showed a saphenous vein with advanced thromboatheromatous degeneration (Fig 2). Diagnosis of a true aneurysm was confirmed by the morphology of the vein within the wall of the aneurysm.

Comment

Saphenous vein grafts are often ligated at the time of orthotopic heart transplantation in patients who have undergone previous coronary artery bypass grafting.

Accepted for publication Feb 11, 1992.

Address reprint requests to Dr Frazier, Texas Heart Institute, PO Box 20345, Houston, TX 77225-0345.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

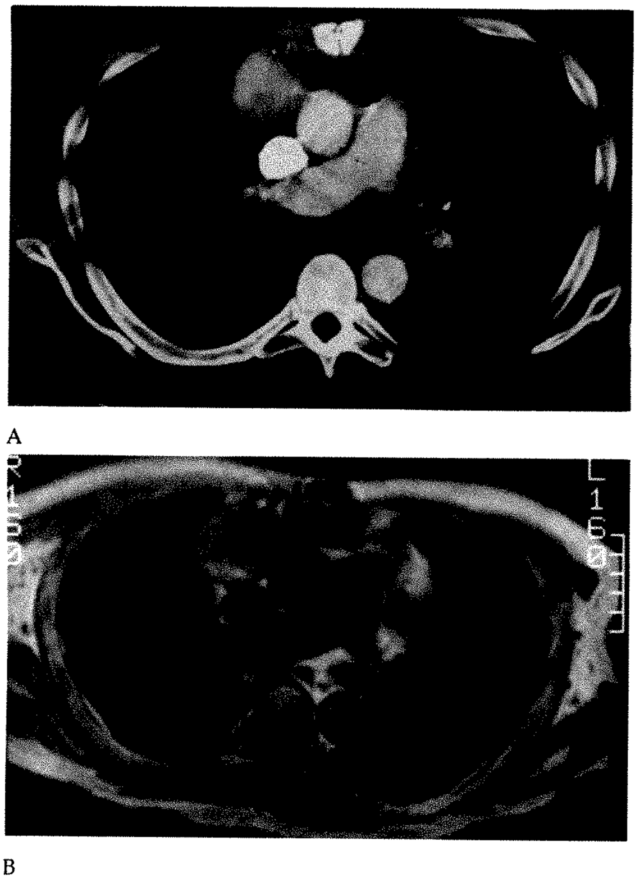


Fig 1. Computed tomogram (A) and magnetic resonance image (B) revealed a contrast-enhancing 5-cm mass adjacent to the ascending aorta.

Graft ligation is also done in patients who require a second myocardial revascularization when the previous grafts have become stenotic or occluded. The proximal graft remnant is frequently left in place if its origin on the ascending aorta is not needed for a subsequent bypass graft. The veins are usually ligated where they are most accessible, and a 1- to 2-cm vein graft stump remains attached to the origin on the ascending aorta. Leaving a short vein remnant is considered safe because it is assumed that this blind-ending pouch will thrombose soon after operation. Thus, it becomes the functional equivalent of oversewing the vein flush with the aorta.

In this patient, it is doubtful that thrombosis and occlusion occurred in the vein stump. Aneurysm formation results from degeneration of the vein graft and an increased intraluminal arterial pressure, which causes increased tangential stress within the wall of the vessel. Immunosuppressive therapy may have contributed to aneurysm formation. We hypothesize that an aneurysm would not have formed had the remnant completely occluded.

Complete excision of the vein graft remnant may have prevented the formation of an aneurysm in this patient; therefore, we recommend that complete excision of accessible vein graft remnants and oversewing of the aortosaphenous anastomoses be considered at the time of orthotopic heart transplantation.

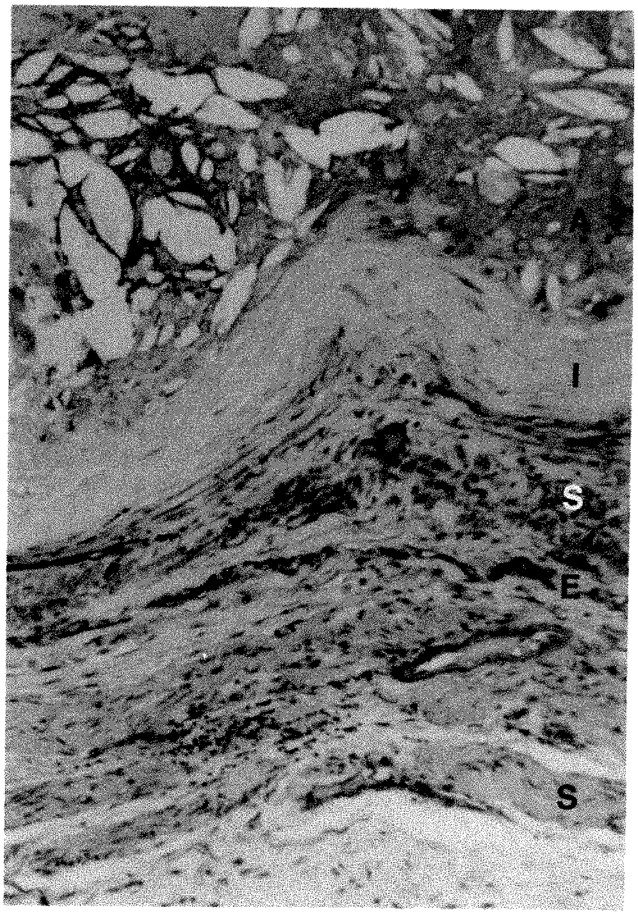


Fig 2. The wall of the aneurysm contains elements of a vein wall: smooth muscle (S) and elastic fibers (E). Note the severe thromboatheromatous degeneration (A) of the hyalinized intima (I). (Movat's pentachrome, ×108 before 29% reduction.)

References

1. Carrasquilla C, Weaver AW. Aneurysm of a saphenous vein graft to common carotid artery. Vasc Surg 1972;6:66–8.
2. Riahi M, Vaser CM, Tomatis LA, Schlossen RJ, Zimmerman G. Aneurysm of saphenous vein bypass graft to coronary artery bypass graft. J Thorac Cardiovasc Surg 1975;70:358–9.
3. Benchimal A, Harris CL, Desser KB, Fleming H. Aneurysm of an aorto–coronary artery saphenous vein bypass graft—a case report. Vasc Surg 1975;9:261–4.
4. Pintar K, Baboriak JJ, Johnson D, Co ED. Atherosclerotic aneurysm in aortocoronary vein graft. Arch Pathol Lab Med 1978;102:287–8.
5. Bramlett DA, Behar VS, Ideker RE. Aneurysm of a saphenous vein bypass graft associated with aneurysms of native coronary arteries. Cathet Cardiovasc Diagn 1982;8:489–94.
6. Shapero LG, Gathaner DF, Swerdloa CD, Wexler L. Rupture of a coronary bypass graft aneurysm: CT evaluation and coil occlusion therapy. AJR 1983;141:1060–2.
7. Murphy JP, Shabb B, Nishikawa A, Adams PA, Walker WE. Rupture of an aortocoronary saphenous vein graft aneurysm. Am J Cardiol 1986;58:555–7.

Chronic, Traumatic Pseudoaneurysm of the Ascending Aorta

Felipe C. Albuquerque, BA, Mark J. Krasna, MD, and Joseph S. McLaughlin, MD

Division of Thoracic and Cardiovascular Surgery, University of Maryland School of Medicine, Baltimore, Maryland

Rupture of the ascending aorta is lethal in virtually all cases. In the recent literature, fewer than 9 cases of chronic, traumatic pseudoaneurysm of the ascending aorta have been documented. Reported herein is such a case, discovered incidentally and repaired successfully under cardiopulmonary bypass using a graft prosthesis. Aortogram remains the diagnostic method of choice in these patients.

(Ann Thorac Surg 1992;54:980–2)

Rupture of the aorta usually occurs after deceleration injury sustained in motor vehicle accidents. Less than 20% of people with this injury survive the event. Two percent of those suffering rupture at the level of the isthmus go on to have development of a chronic aneurysm [1]. Rupture at the level of the aortic root is virtually uniformly fatal secondary to instantaneous cardiac tamponade and other associated cardiac injuries [2]. Reported is a case of pseudoaneurysm of the ascending aorta successfully repaired using cardiopulmonary bypass.

A 34-year-old man suffered a gunshot wound to the left precordium on January 12, 1991, after which he underwent emergent median sternotomy (at another hospital) for relief of acute pericardial tamponade. The bullet, located within the myocardium of the right ventricle, was not removed because the operating room was not equipped for cardiopulmonary bypass. At that time, a large, stable aneurysm of the ascending aorta was noted. Computed tomographic scan 2 days postoperatively showed an aneurysm of the ascending aorta arising above the level of the aortic valve (Fig 1). A sagittal magnetic resonance image revealed bilateral pleural effusions.

Transfemoral aortogram demonstrated a secular aneurysm approximately 7 cm × 9 cm originating 2 cm above the coronary ostia (Figs 2, 3).

Upon admission to University of Maryland, the patient reported a medical history significant for three motor vehicle accidents (1979, 1980, and 1990), during which the patient suffered fractures of several ribs and a right pneumothorax. The patient denied a history of sexually transmitted disease (including syphilis), hypertension, or familial illnesses.

The physical examination and laboratory tests were within normal limits. An electrocardiogram showed normal sinus rhythm with an incomplete right bundle-branch block. A chest roentgenogram showed a slightly widened mediastinum, a normal cardiac silhouette, a bullet near the apex of the heart, and normal lung fields.

On February 8, 1991, a median sternotomy was performed through the previous incision, which revealed a 7 cm × 7 cm aneurysm, 2 cm above the aortic valve. After the patient was placed on femoral cardiopulmonary bypass and the left ventricle was decompressed, the aorta was cross-clamped and retrograde cardioplegia injected. The aneurysm was entered, demonstrating a false lumen arising from the aorta 3 cm above the coronary ostia. The aneurysm was resected and a 24-mm Dacron graft, previously autoclaved in plasma, was selected to bridge the site. The proximal anastomosis was performed first using 2-0 Ethibond (Ethicon, Somerville, NJ) pledgeted, interrupted mattress sutures. The distal anastomosis was completed by running 3-0 Prolene (Ethicon) sutures buttressed by Teflon strips. At this point, the apex of the heart was elevated and the bullet removed. The patient was weaned off bypass without complication. He did well after operation and was discharged on postoperative day 7.

Comment

Deceleration injuries are likely to occur at the level of the ligamentum arteriosum, where the relatively mobile heart and arch join the fixed descending aorta. Nevertheless, displacement of the heart into the left posterior chest can subject the ascending aorta to torsion, accounting for the relative frequency of rupture in this area. The likelihood of concomitant valvular and cardiac damage with ascending aortic rupture, however, makes it far less likely that a patient will survive the initial traumatic event and go on to have development of a chronic pseudoaneurysm [3]. Indeed, in their review of the literature spanning 1950 to 1980, Finkelmeier and associates [2] report fewer than 9 cases (3% of a total of 284) of chronic, traumatic aneurysm arising above the aortic valve [2]. Recently, dissections occurring after cardiac operations have become the leading cause of ascending aortic dissection.

In the case reported herein, both the histology and the history confirm the presence of a chronic pseudoaneurysm. A chronic aneurysm is defined as one that persists longer than 3 months after the original traumatic event. Such is the case for this patient, whose most recent motor vehicle accident preceded the diagnosis of his aneurysm

---

Accepted for publication Feb 12, 1992.

Address reprint requests to Dr Krasna, Division of Thoracic and Cardiovascular Surgery, University of Maryland Hospital, 22 S. Greene St, Baltimore, MD 21201.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

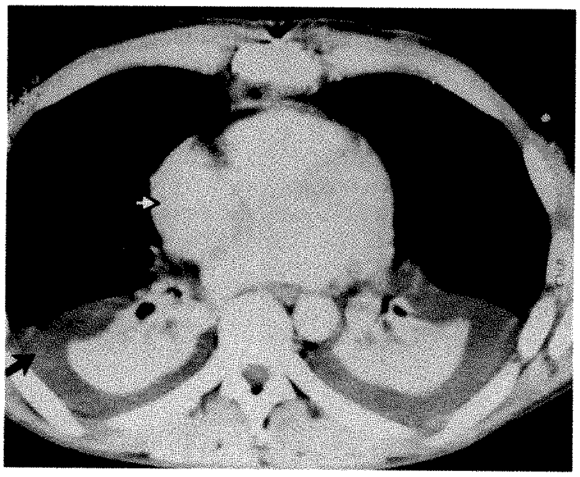


*Fig 1. Computed tomographic scan of the chest showing bilateral pleural effusions (*black arrow*) and enlarged ascending aorta (*white arrow*).*

by 5 months. Pseudoaneurysms, unlike true aneurysm, are contained only within a thin layer of adventitia and not by the natural sequelae of such lesions [4]. Pathologic examination of our patient's aorta revealed a false, saccular pouch consisting only of fibrous tissue.

Considering the lethality of rupture, early diagnosis of an aortic aneurysm is imperative. Symptoms associated with enlarging aneurysms include pain, dyspnea, cough, and hoarseness. Without these symptoms, the presence of a widened mediastinum on chest roentgenogram is the initial diagnostic clue. The definitive diagnosis is made, however, through the use of aortography, which will delineate not only the aneurysmal site but the anatomy of adjacent sections of the aorta as well. The latter is especially critical in cases involving the aortic arch and bifurcation. Other methods of diagnosis include the use of Doppler echocardiography and computed tomography [5, 6]. The primary advantage of these modes is their noninvasiveness, which may be of importance when assessing the acutely traumatized patient.

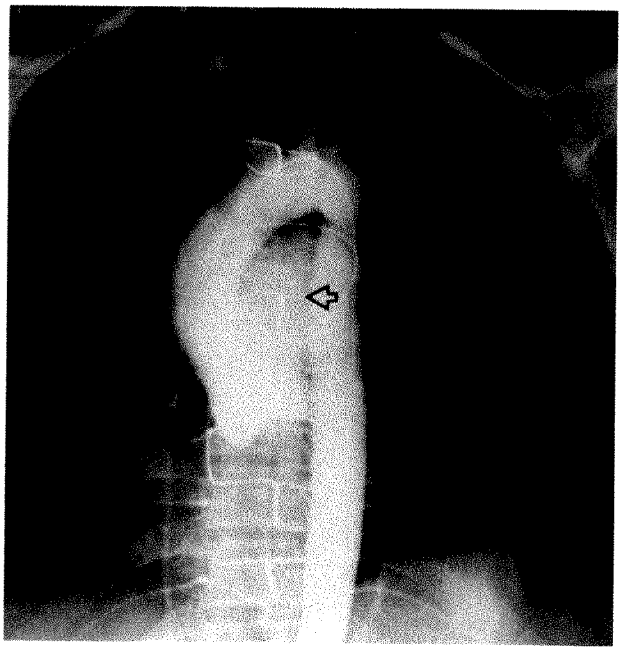


*Fig 2. Anteroposterior aortogram demonstrating large ascending aortic pseudoaneurysm medial to the left edge of the ascending aorta (*arrow*).*

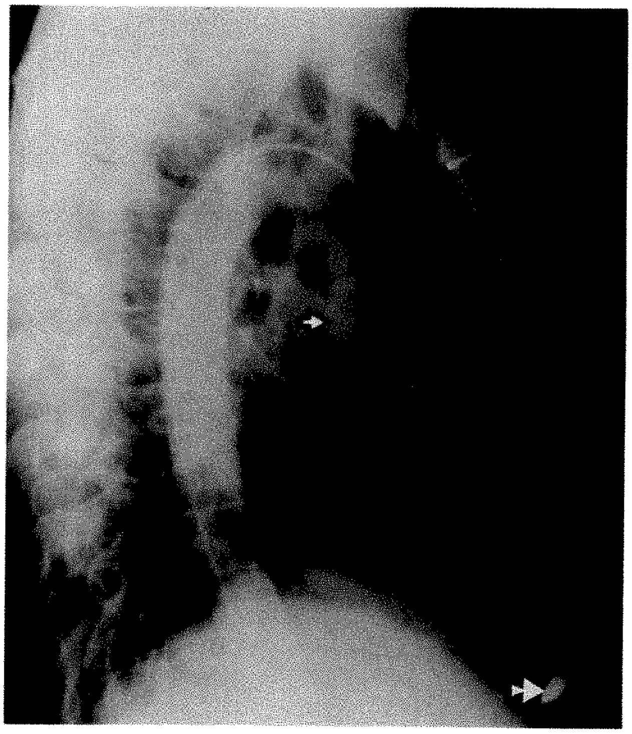


*Fig 3. Lateral aortogram showing aneurysm (*upper arrow*) and bullet (*lower arrow*).*

Based on their proclivity to rupture even several years after development, traumatic pseudoaneurysms of the aorta are treated with excision and prosthetic repair [7]. In 1956, Cooley and De Bakey [8] became the first to repair a chronic, traumatic pseudoaneurysm of the ascending aorta. Their work, as well as the successful outcome of the patient described herein, confirms that chronic aneurysms of the ascending aorta can be managed safely through operative intervention.

Given the few cases of chronic, posttraumatic aneurysms of the ascending aorta, it is difficult to quantitate the risk of death from operation versus that of delayed rupture. Nevertheless, data on patients with chronic aneurysms of the descending aorta suggest that the mortality rate is far less for surgical repair than for delayed rupture (4.6% versus 33%, respectively) [2].

References

1. Parmley LF, Mattingly TW, Manion WC, Jahnke EF. Nonpenetrating traumatic injury of the aorta. Circulation 1958;17: 1086–101.

2. Finkelmeier BA, Mentzer RM, Kaiser DL, Tegtmeyer CJ, Nolan SP. Chronic traumatic thoracic aneurysm: influence of operative treatment on natural history. An analysis of reported cases, 1950–1980. J Thorac Cardiovasc Surg 1983;84: 257–66.
3. Schwartz ML, Fisher R, Sako Y, Castaneda AR, Grage TB, Nicoloff DM. Post-traumatic aneurysms of the thoracic aorta. Surgery 1975;78:589–93.
4. Bennett DE, Cherry JK. The natural history of traumatic aneurysms of the aorta. Surgery 1967;61:516–23.
5. Moya JL, de Pablo C, Sanchez M, Barrios V, Fraj J, Asin-Cardiel E. Traumatic rupture of aorta: diagnosis by Doppler echocardiography. Chest 1990;98:1016–7.
6. White RD, Lipton MJ, Higgins CB, et al. Noninvasive evaluation of suspected thoracic aortic disease by contrast-enhanced computed tomography. Am J Cardiol 1986;57: 282–90.
7. Cooley DA. Aneurysms of the ascending aorta: surgical treatment using hypothermic arrest. Cardiology 1990;77:373–87.
8. Cooley DA, De Bakey ME. Resection of entire ascending aorta in fusiform aneurysm using cardiac bypass. JAMA 1956;162: 1158–9.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1995 may begin the recertification process in 1993. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is May 1, 1993. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Aneurysm of the Ascending Aorta After Cardiac Transplantation

Jean-Olivier Defraigne, MD, Olivier Vahdat, MD, Jean-Paul Lavigne, MD,
Jean-Claude Demoulin, MD, PhD, and Raymond Limet, MD, PhD

Departments of Cardiovascular Surgery and Cardiology, C.H.U. Sart-Tilman, Liege, Belgium

We report the case of a 57-year-old female cardiac transplant patient in whom an aneurysm of the recipient side of the ascending aorta developed 1 year after transplantation. Although a mycotic origin was the likely cause, histologic examination diagnosed an atherosclerotic aneurysm.

(Ann Thorac Surg 1992;54:983–4)

After cardiac transplantation, infection and rejection remain the major causes of morbidity and death [1, 2]. Besides infection, immunosuppression itself accounts for some morbidity [1, 3]. Immunosuppressive agents have deleterious side effects that may alter both quality of life and survival. However, graft atherosclerosis appears progressively as a major impediment to long-term survival [4, 5]. We present here a case of an aneurysm of the ascending aorta that appeared within the first year after transplantation. The immunosuppressive regimen could have been a contributive factor for rapid development of this aneurysm.

A 57-year-old woman underwent transplantation for ischemic cardiomyopathy. The donor aorta was normal. The diameter of the recipient aorta was 35 mm, and there was no evidence of atherosclerotic plaque formation. Immunotherapy included azathioprine, cyclosporin, and prednisone. The postoperative course was complicated by right pleural empyema successfully treated with intensive antibiotic therapy and drainage.

At 5 months, a stage IIB rejection required increased dosages of corticoid. Muscular atrophy, systemic hypertension, hypercholesterolemia, and insulin-dependent diabetes occurred as side effects of immunotherapy.

After 8 months, a decompensation of the diabetes occurred, and several temperature peaks were noted. Although chest roentgenograms and cultures of sputum and urine had negative results, she was treated with broad-spectrum antibiotics.

Two months later, a right basal bronchopneumonia and left lower limb edema developed, with purulent cutaneous necrosis in the anterolateral region of the left leg. *Serratia marcescens* and *Proteus vulgaris* were isolated from the exudate. At this time, she complained of retrosternal chest pain. On chest roentgenogram, the upper mediastinum was widened with loss of the mediastinal border of the right upper lobe (Fig 1). An aneurysm of the ascending aorta was demonstrated on computed tomographic scan of the chest (Fig 2) and confirmed on aortography (Fig 3).

The left femoral vessels were cannulated for cardiopulmonary bypass. After sternotomy, a saccular aneurysm was discovered, located on the right anterolateral side of the recipient ascending aorta, 2 cm above the suture line. The wall of the donor aorta appeared normal, whereas the wall of the recipient aorta was severely atherosclerotic.

After cross-clamping of the aorta and cold cardioplegia (St. Thomas'), the aneurysm was resected and a patch of collagenated Dacron sutured over the defect. The patient was easily weaned from cardiopulmonary bypass and was extubated after 24 hours. Major sepsis occurred due to bilateral confluent bronchopneumonia 3 days postoperatively. Refractory hypoxemia caused death on day 4.

Histologic examination of the aneurysm showed fibrous thickening of the intima and rarefaction of the media, consistent with atherosclerosis. No signs of mycotic aneurysm or of an inflammatory response could be detected. The cultures of the aortic wall had negative results. Postmortem examination was not obtained because of family refusal.

Comment

Infection remains a major cause of morbidity and mortality after heart transplantation. Considering the previous empyema, repeated bronchopneumonia, and febrile episodes, and particularly the pyodermitis of the left leg, a mycotic origin could have been considered the most likely cause for aneurysm formation. This pyodermitis could be consecutive to septic embolization from the aneurysm. Nevertheless, histologic examination failed to demonstrate inflammatory infiltration of the arterial wall, and the cultures of the aneurysm wall had negative results, although previous antibiotic therapy could be responsible for this. Surprisingly the anatomopathologic findings were consistent with atherosclerosis of the recipient aorta.

Minick and associates [6] induced atherosclerosis in rabbits after exposure to an allergic injury and lipid-enriched diet. Nevertheless, the relevance of animal models to human disease is not clear. Graft atherosclerosis is not entirely related to the risk factors classically considered for the development of "ordinary" coronary artery disease [6, 7]. It is considered to be a consequence of

---

Accepted for publication Feb 13, 1992.

Address reprint requests to Dr Limet, Service de Chirurgie Cardio-Vasculaire, C.H.U. du Sart-Tilman, 4000 Liege, Belgium.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Fig 1. Chest roentgenogram shows widening of the superior mediastinum with loss of the right mediastinal border.

initial immune injury of the coronary endothelium with exposure of a thrombogenic surface. Subsequent platelet exposition and lipid infiltration lead to fibrous tissue accumulation and to intimal thickening. In a multivariate analysis, mismatches at the HLA-A2 locus and elevated serum triglyceride levels (but not cholesterol levels) were suggested as associated factors [4, 5]. However, the pathogenesis of graft atherosclerosis is not well understood and may eventually be considered to be a manifestation of chronic rejection [7].

In our case, the localization of the aneurysm on the recipient aorta eliminates an immunological origin. In contrast, our patient, who initially underwent transplantation for ischemic cardiomyopathy, was predisposed to the development of such an atherosclerotic aneurysm. At time of the graft, the risk factors included non–insulin-dependent diabetes mellitus and mild hypertension [8]. After transplantation, all these factors were aggravated. With cyclosporin therapy, the hypertension worsened [8]. Hypercholesterolemia and loss of control of diabetes occurred as a consequence of corticotherapy [7]. After the transplantation, improvement of cardiac output increased the shear stresses on the ascending aorta. Combinations of these factors, to varying degrees, could explain the development of accelerated atherosclerosis in the recipient aorta, with consequent rapid growth of the aneurysm until the time of operation [8]. Nevertheless, on a clinical ground, a mycotic origin was the likely origin but was not confirmed by histopathologic examination.

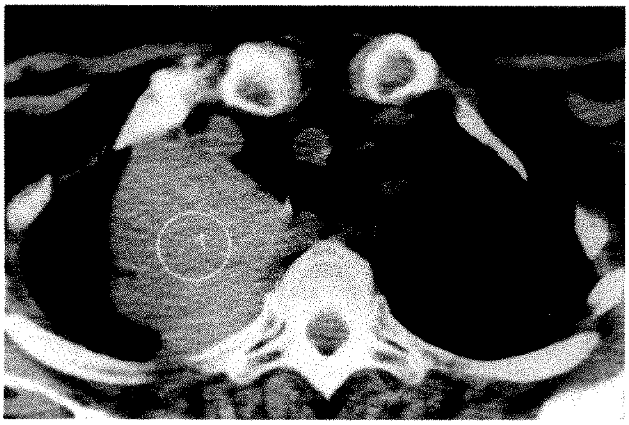


Fig 2. Computed tomographic scan shows an aneurysm of the ascending aorta (arrow).

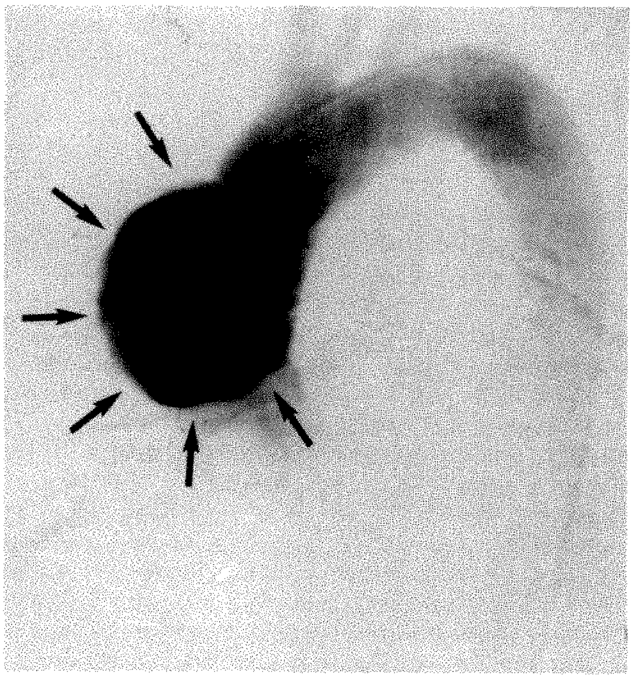


Fig 3. Angiogram shows the aneurysm originating from the right side of the ascending aorta.

References

1. Cabrol C, Gandjbakhch J, Pairie A, Cabrol A, Mattei MF, Leger P. Heart transplantation in Paris, at "La Pitié Hospital." Heart Transplant 1985;4:476–80.
2. Kaye MP. The international heart transplant registry. First official report. Heart Transplant 1984;3:278–83.
3. Baumgartner WA. Infections in cardiac transplantation. Heart Transplant 1983;3:75–80.
4. Zusman DR, Stinson EB, Oyer PE, et al. Determinants of accelerated graft atherosclerosis (AGAS) in conventional and cyclosporine treated heart transplant recipients [Abstract]. J Heart Transplant 1985;4:587.
5. Taylor DO, Thompson JA, Hastillo A, et al. Hyperlipidemia after clinical heart transplantation. J Heart Transplant 1989;8: 209–13.
6. Minick R, Stermeman MB, Insull W. Role of endothelium and hypercholesterolemia in intimal thickening and lipid accumulation. Am J Pathol 1979;85:131–51.
7. Hess ML, Hastillo A, Mohanahumar T, et al. Accelerated atherosclerosis in cardiac transplantation: role of cytotoxic B-cell antibodies and hyperlipidemia. Circulation 1983; 68(Suppl 2):94–101.
8. Castelli WP. Cardiovascular disease and multifactorial risk: challenge of the 1980s. Am Heart J 1983;106:1191–200.

Simplified Correction of Outflow Obstruction After Mitral Valve Replacement

Mark K. Reed, MD, and Leigh I. G. Iverson, MD

Department of Surgery, David Grant USAF Medical Center, Travis Air Force Base, California; and East Bay Heart Surgery, Oakland, California

Left ventricular outflow tract obstruction after mitral valve replacement may occur when a retained native anterior leaflet prolapses between prosthetic struts. Existing reports of left ventricular outflow tract obstruction by this mechanism lack emphasis on its surgical treatment. We obtained definitive relief of left ventricular outflow tract obstruction by transaortic exposure, division, and partial excision of the obstructing leaflet. This approach minimizes the complexity and potential morbidity of the correction.

(Ann Thorac Surg 1992;54:985–6)

Surgical treatment of mitral valve dysfunction preferentially preserves native tissue [1]. When the anatomic exigencies mandate replacement, the mitral apparatus ought to be left intact to preserve left ventricular function [2, 3]. Valve preservation, however, harbors the potential for postoperative "sailing" of the native anterior leaflet with resultant left ventricular outflow tract obstruction (LVOTO). Previous reports of this complication have concerned its diagnosis more than its surgical treatment [4–6]. We describe an expedient operative approach successfully used for 2 patients, 1 with severe acute postoperative LVOTO and the other with milder chronic LVOTO and secondary atrial fibrillation.

Case Reports

Patient 1

A 74-year-old man was admitted with atrial fibrillation and congestive failure. Echocardiography showed left atrial and ventricular dilatation (6.9 and 5.9 cm end-diastolic dimensions, respectively) with mild aortic and severe mitral valve insufficiency. Catheterization revealed normal coronary arteries. At operation the native mitral valve was found to have myxomatous, billowing leaflets and ruptured chordae of the posterior leaflet. A portion of the excessive posterior leaflet with associated chordae fragments was removed, whereas the remaining valvular structures were left unaltered. A No. 33 Carpentier-Edwards porcine heterograft was secured in the supraannular position with the valve sutures plicating the redundant anterior leaflet.

Postoperatively, atrial fibrillation and a prominent systolic murmur prompted echocardiography showing systolic LVOTO with a gradient of 4.5 m/s (80 to 90 mm Hg). The patient was managed medically for 21 months but refractory atrial fibrillation and progressive exersional dyspnea mandated reoperation. Dissection was limited to that needed for exposure of the right atrium and the ascending aorta. The aorta was opened, and through the retracted aortic valve could be seen the anterior native mitral leaflet stretched between struts of the prosthesis. A resection limited to this portion along with corresponding chordae was accomplished. Subsequent echo studies have documented normal prosthetic valve function without outflow tract obstruction, although the rhythm remains atrial fibrillation.

Patient 2

A 69-year-old man with known aortic and mitral regurgitation was admitted with unstable angina and congestive heart failure. Echocardiography showed dilatation of the left atrium and left ventricle (5.3 and 6.0 cm end-diastolic dimensions, respectively) with a normal ejection fraction. The septum was 2.0 cm thick without abnormal motion. Catheterization showed severe mitral regurgitation and two-vessel coronary stenosis. At operation, saphenous vein grafts to the left anterior descending and right coronary arteries were performed. The mitral leaflets were highly redundant with greatly elongated chordae. A No. 31 Carpentier-Edwards porcine valve was placed in the supraannular position without excision of native valve structures. Anchoring sutures were directed through part of the extraneous anterior leaflet as we intended them to plicate it against the annulus.

Postoperatively there was a harsh systolic murmur and a state of low cardiac output. Echocardiography and catheterization demonstrated severe systolic LVOTO prompting the patient's return to the operating room. The aorta was opened below the grafts. Through the aortic valve, prosthetic struts were seen pressing the native anterior mitral leaflet against the septum. Transaortic resection of the obstructing tissue eliminated LVOTO. At 2 years' follow-up, although remaining in atrial fibrillation, he is asymptomatic.

Comment

Left ventricular outflow tract obstruction is a well-recognized, albeit uncommon complication, of prosthetic valve placement in the mitral position. In years past, when the standard procedure for mitral valve replacement included excision of the native mitral leaflets and chordae, an oversized prosthetic valve relative to the receiving annulus was the typical cause of LVOTO after

---

Accepted for publication Feb 14, 1992.

Address reprint requests to Dr Iverson, East Bay Heart Surgery, 365 Hawthorne Ave, Suite 301, Oakland, CA 94609-3102.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

mitral valve replacement [7, 8]. Although it is now generally believed that the optimal left ventricular systolic pump function requires an intact mitral subvalvular apparatus [2, 3], an unaltered redundant anterior leaflet is liable to prolapse between prosthetic struts during systole with resultant LVOTO. Undoubtably, prevention is the best treatment. Techniques such as those described by David [9] preserve ventricular function while minimizing the likelihood of prosthetic-valve–associated LVOTO. These entail partial excision of excessive leaflet tissue, resuspension of the commissural edges, and the use of smaller valves with central flow. With these operative refinements, the occurrence of prosthetic-valve–associated LVOTO should become a rarity. Nonetheless, LVOTO needs to be considered in patients with a wide range of hemodynamic disturbances and an unexpected murmur after mitral valve replacement.

Previous descriptions of interstrut prolapse of the mitral septal leaflet have aptly depicted its clinical variations and echocardiographic features but have not emphasized its surgical treatment [3–5]. At one extreme, exemplified by our second case, is severe acute low output failure. Much milder, yet not inconsequential obstruction was manifested by refractory atrial fibrillation in the first case. Survival of patients in the former category clearly requires prompt surgical intervention. On the other hand, those whose obstruction is less severe may have insidious development of left ventricular failure with the long-term risks and functional impairment of chronic atrial fibrillation.

In either case, we advocate transaortic exposure with division and excision of the obstructive mitral leaflet, which has proved to be an expeditious corrective procedure. Particularly advantageous for minimizing the morbidity of reoperation is the avoidance of dissection other than that needed to establish bypass. Without atriotomy, mechanical trauma to the previously operated heart is further diminished. Although such a limited approach raises serious concerns regarding de-aeration and venting, in practice these proved not to be difficulties. Should there yet be patients receiving medical management of this complication, we recommend they be considered candidates for surgical treatment using the approach we have outlined.

References

1. Livesay JJ, Talledo OJ. The current preference for mitral valve reconstruction. Tex Heart Inst J 1991;18:87–92.
2. Spence PA, Peniston CM, David TE, et al. Toward a better understanding of left ventricular dysfunction after mitral valve replacement: an experimental study with possible clinical implications. Ann Thorac Surg 1986;41:363–71.
3. Yun KL, Fann JI, Rahill SC, et al. Importance of the mitral subvalvular apparatus for left ventricular segmental systolic mechanics. Circulation 1990;82(Suppl 5):89–104.
4. Come PC, Riley MF, Weintraub RM, et al. Dynamic left ventricular outflow tract obstruction when the anterior leaflet is retained at prosthetic mitral valve replacement. Ann Thorac Surg 1987;43:561–3.
5. Jacobs LE, Kotler MN, Ioli A. Left ventricular outflow tract obstruction following mitral valve replacement with Carpentier-Edwards prosthesis. Echocardiography 1990;7:147–53.
6. Roberts WC, Dollar AL. Extreme obstruction to left ventricular outflow by a bioprosthesis in the mitral valve position. Am Heart J 1991;121:607–8.
7. Jett GK, Jett MD, Barnhart GR, van Rijk-Swikker GL, Jones M, Clark RE. Left ventricular outflow tract obstruction with mitral valve replacement in small ventricular cavities. Ann Thorac Surg 1986;41:70–4.
8. Cohn LH. Complications related to mitral valve surgery. In: Waldhausen JA, Orringer MB, eds. Complications in cardiothoracic surgery. St. Louis: Mosby-Year Book, 1991:251.
9. David TE. Mitral valve replacement with preservation of chordae tendinae: rationale and technical considerations. Ann Thorac Surg 1986;41:680–2.

INVITED COMMENTARY

As mentioned by Reed and Iverson in their article, I agree that "prevention is the best treatment" of left ventricular outflow tract obstruction after mitral valve replacement with preservation of chordae tendineae. The operative technique they described to manage those 2 patients is logical, and it is simpler, safer, and more economical than mitral valve rereplacement. However, I believe that the important message in their article is to avoid this complication. A triangular resection of the anterior leaflet of the mitral valve with resuspension of the chordae tendineae is all that is required to prevent this problem (see reference [9]).

The mitral apparatus is pulled toward the ventricular cavity during systole in patients with intact chordae tendineae because of contraction of the walls subtended by the papillary muscles. Consequently, the leaflets of the mitral valve may cause dynamic obstruction of the outflow tract in certain patients. This may occur after mitral valve repair for mitral regurgitation or after mitral valve replacement with preservation of the anterior leaflet. Malorientation of a porcine bioprosthesis during mitral valve replacement may also cause obstruction of the outflow tract. Avoidance of plication of the mitral annulus in a single area after partial resection of a prolapsing segment of the posterior leaflet prevents outflow tract obstruction after mitral valve repair; partial resection of the anterior leaflet and correct orientation of a bioprosthetic valve prevent this complication after mitral valve replacement.

Tirone E. David, MD

Division of Cardiovascular Surgery
The Toronto Hospital
200 Elizabeth Street, 13 EN - 222
Toronto, Ontario
M5G 2C4, Canada

Bronchoenteric Fistula From an Infected Internal Cardioverter Defibrillator

Peter L. Birnbaum, MD, Samuel V. Lichtenstein, MD, PhD, William H. Noble, MD,
Benjamin G. Guslits, MD, Brian D. Kenney, MD, D. Ian Soutter, MD,
Anthony L. Panos, MD, Paul Dorian, MD, and David Newman, MD

Divisions of Cardiovascular Surgery, Anaesthesia, General Surgery, and Cardiology, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

The case of a transdiaphragmatic bronchoenteric fistula from an infected internal cardioverter defibrillator is presented.

(Ann Thorac Surg 1992;54:987–8)

The development of the automatic implantable cardioverter and defibrillator (ICD) has provided an important tool for the management of patients with life-threatening ventricular arrhythmias. Since the introduction of this device, various reports have identified associated infectious complications [1, 2]. This case report documents the presentation and management of a bronchoenteric fistula from an infected ICD device.

A 47-year-old woman with steroid-dependent asthma sustained an episode of primary ventricular fibrillation in 1987. No reversible causes for ventricular fibrillation were found, and all cardiac investigations were normal. Polymorphic ventricular tachycardia was induced with triple extrastimuli at an invasive electrophysiologic study. An ICD (Ventak model 1520; Cardiac Pacemakers Inc, St. Paul, MN) was inserted. A left anterolateral thoracotomy was used for placing extrapericardial patches anteriorly and posteriorly, which were secured with interrupted nonabsorbable sutures. The ICD was positioned retrorectus in the anterior abdominal wall.

Eight months before her current admission, a pulse generator pocket infection developed, documented by gallium and computed tomographic scans [3, 4]. The preoperative chest roentgenogram demonstrated the patches to be in good position. The pulse generator was removed, but thoracotomy for removal of the patches was deferred because of the severity of her asthma. No systemic signs or symptoms of infection were present. Cultures of the generator pocket grew oral anaerobes. The patient was treated with 4 weeks of intravenous antibiotics and a further 4 weeks of oral therapy. Continuous oral antibiotic therapy had to be discontinued because of gastrointestinal intolerance.

Five months before admission, recurring episodes of coughing and vomiting developed, especially at night. The patient also had severe constipation, necessitating care at the emergency department of another hospital. A roentgenogram showed a pericardial patch inside the colon (Fig 1). Relief was obtained after a Fleet enema and an explosive bowel movement.

Intermittent febrile episodes prompted the current admission for ICD patch removal by thoracotomy. The patient was asymptomatic of any bronchoenteric communication. Preoperative chest roentgenogram showed only the anterior patch. The procedure was complicated by dense fibrous adhesions involving the diaphragm, the heart, and the lower lobe of the left lung. Abscess pockets were identified enveloping the patch and electrode leads. After tedious dissection two sensing electrodes and one patch were removed. Thorough dissection around the pericardial surface of the heart failed to reveal any remnants of the posterior patch or a fistula.

On the morning of the first postoperative day the patient's status was unremarkable. Several hours later she suffered a respiratory arrest believed secondary to gastric aspiration. After resuscitation, including intubation and ventilation, the patient was transferred to the intensive care unit. A nasogastric tube was placed and its position confirmed. It continued to bubble synchronously with the inspiratory cycle of the ventilator. Using the in-line oxygen monitor from the ventilator, the expired gas from the nasogastric tube was found to have the same concentration of oxygen as the ventilator (100%). Bronchoscopy failed to show any evidence of a bronchogastric or esophageal communication. Double-lumen endotracheal intubation localized and isolated the fistulous communication to the left lung. A contrast esophagogram failed to identify any communication with the tracheobronchial tree. The patient remained intubated with the double-lumen endotracheal tube, and independent lung ventilation was continued. Ventilatory management was complicated by pulmonary hypertension and a serious air leak into the stomach. Simultaneously bronchoscopy and gastroscopy with methylene blue injection into the left lower lobe bronchus identified a communication to the gastric fundus.

The patient was returned to the operating room for repair of the bronchoenteric fistula. A thoracotomy was performed to avoid contamination of the peritoneal cavity and provide easier access to the bronchial side of the fistula. Careful dissection between the diaphragmatic

---

Accepted for publication Feb 17, 1992.

Address reprint requests to Dr Lichtenstein, Rm 304B, St. Michael's Hospital, 30 Bond St, Toronto, Ont, Canada M5B 1W8.

© 1992 by The Society of Thoracic Surgeons 0003-4975/92/$5.00

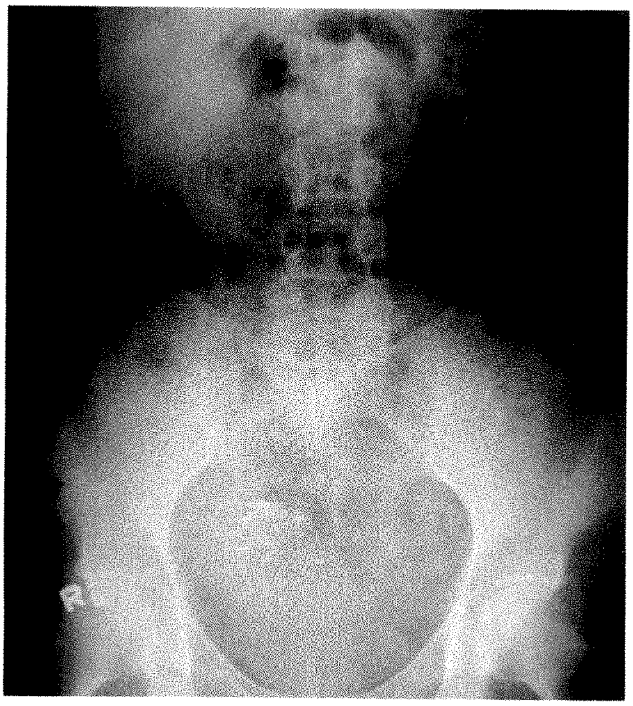


Fig 1. *Erect radiograph of abdomen with internal cardioverter defibrillator patch in colon.*

surface of the heart, the diaphragm itself, and the left lower lobe identified the bronchogastric fistula. The high-velocity bronchial leak was sutured primarily. The defect in the fundus of the stomach was repaired transdiaphragmatically, with an omental pedicle interposed between fundus and diaphragm.

The postoperative recovery was gradual, requiring prolonged intubation. At 5 months' follow-up the patient was well with no signs of infection or arrhythmias.

Comment

We surmise that infection of the posterior patch with steroid dependence was responsible for the bronchogastric fistula. After removal of the ICD generator, the posterior patch was free to migrate and fistulize to the gastrointestinal tract and eventually was passed per rectum.

This patient's entire course was substantially complicated by her steroid-dependent asthma. It was vital that the bronchogastric communication be identified quickly after her respiratory arrest because of continuous pulmonary soiling from acid aspiration and destruction of already compromised asthmatic lungs. We attempted to minimize lung injury from aspiration with a head-up position and various modes of ventilation. However, it soon became obvious that primary closure of the fistula was required to prevent further contamination of the lung and permit adequate ventilation in the face of a large lung leak and high airway pressures.

Foreign body infections may range from localized pocket infections to severe life-threatening sepsis. Experience with pacemaker complications has demonstrated that infections may become locally invasive and result in migration of the pulse generator beyond its usual anatomic location. This has resulted in the rare finding of an intragastric [5] and intracolonic [6] cardiac pacemaker. Siclari and colleagues [7] reported erosion of an ICD patch through the right ventricular free wall, necessitating cardiopulmonary bypass for patch removal and right ventricular reconstruction. The migration of the ICD patch in our patient from the thorax transdiaphragmatically into the gastric fundus was permitted by staging of the procedures to remove the pulse generator and the patches. Although reports have demonstrated nonoperative treatment of ICD infections [8], patients with steroid dependence may be better served by complete explantation of all hardware in a single-staged procedure.

References

1. Furman S. Implantable cardioverter defibrillator infection. PACE 1990;13:1351.
2. Wunderly D, Maloney J, Edel T, McHenry M, McCarthy PM. Infections in implantable cardioverter defibrillator patients. PACE 1990;13:1360–4.
3. Goodman LR, Amassi GH, Troup PH, et al. Complications of automatic implantable cardioverter defibrillators: radiographic, CT, and echocardiographic evaluation. Radiology 1989;170:447–52.
4. Kelly PA, Wallace S, Tucker B, et al. Postoperative infection with the automatic implantable cardioverter defibrillator: clinical presentation and use of the gallium scan in diagnosis. PACE 1988;11:1220–5.
5. Samaan HA. An intragastric cardiac pacemaker. Thorax 1973; 28:113–4.
6. Siclari F, Uhlschmid G, Zwicky P, Turina M. Intracolonic migration of a pacemaker generator. Thorac Cardiovasc Surg 1986;34:338–9.
7. Siclari F, Klein H, Troster J. Intraventricular migration of an ICD patch. PACE 1990;13:1356–9.
8. Taylor RL, Cohen DJ, Widman LE, Chilton RJ, O'Rourke RA. Infection of an implantable cardioverter defibrillator: management without removal of the device in selected cases. PACE 1990;13:1352–5.

Total Correction of Transposition of Great Arteries With Atrioventricular Septal Defect

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Neil Wilson, MRCP, DCH,
Zohair Al Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

A successful anatomical correction of transposition of the great arteries with an atrioventricular septal defect is reported. This combination of anomalies is rare, and the anatomical correction is unusual in that the operation involves all four heart valves.

(Ann Thorac Surg 1992;54:989–90)

The association of atrioventricular septal defects with transposition of the great arteries (d-TGA) is rare [1–3]. These anomalies usually coexist with pulmonary stenosis or pulmonary atresia [3]. Unrestricted pulmonary blood flow is seldom seen in this complex of anomalies. We report a total anatomical correction in a patient with TGA and an atrioventricular septal defect (AVSD) with unrestricted pulmonary blood flow using the arterial switch procedure and a two-patch repair of the AVSD.

A 9-year-old girl was admitted with mild cyanosis apparently present from the age of 3 years. She was reasonably grown with height and weight on the 25th centile. Auscultation revealed a loud second heart sound with grade 3/6 systolic murmur and a soft diastolic grade 2/6 rumble in the third and fourth intercostal space of the left parasternal region.

Electrocardiogram revealed left-axis deviation with biventricular hypertrophy. Chest roentgenogram showed moderate cardiomegaly (cardiothoracic ratio, 26/36) with pulmonary plethora. Echocardiography and cardiac catheterization demonstrated situs solitus, atrioventricular concordance, and ventriculoarterial discordance with a well-developed confluent AVSD. There was a 16% increase in oxygen saturation in the right atrium with a further 8% increase in the right ventricle. The ventricular pressures were equalized (93/2 mm Hg), and the pulmonary artery pressure was at systemic level (84/55 mm Hg; mean, 65 mm Hg).

Operation was performed using standard cardiopulmonary bypass techniques and systemic hypothermia at 20°C. The aorta was anterior to and to the right of the pulmonary artery. The main pulmonary artery was dilated to three times the size of the aorta. The right coronary and the left anterior descending coronary arteries arose together from the left sinus, and a separate circumflex artery was found arising from the right sinus. There was an intermediate form of AVSD [3] with no cleft in the anterior leaflet of the mitral portion of the atrioventricular valve (Fig 1). Between the anterior portion of the mitral and tricuspid valves and the posterior leaflets of the mitral and tricuspid valves there was a layer of tissue on the summit of the ventricular septum with a well-developed ventricular septal defect.

Repair of the AVSD was done using the two-patch technique with two separate, fashioned bovine pericardial patches (Ionescu-Shiley, Irvine, CA) for closure of the ventricular and atrial components of the defect. The atrioventricular valve orifices were of adequate size and competence was achieved with minimal repair of the bridging leaflets at the point of attachment to the patch. The transposed great arteries were corrected by an arterial switch procedure with coronary transfer. The pulmonary artery was repositioned to the anterior root using the Le Compte maneuver. The coronary transfer was effected with a button of the aortic wall to the neoaortic root. The resulting defect in the neopulmonary root was repaired with a pantaloon-shaped bovine pericardial patch. The discrepancy in the size of the distal aorta to the neoaortic root was managed by adjusting the suture line and performing an anterior, vertical aortotomy to increase the sewing length of the distal aorta. It was possible to complete the anastamosis without use of prosthetic material.

The patient was weaned from cardiopulmonary bypass with minimal inotropic support. Prostaglandin infusion was commenced prophylactically to obviate elevation of pulmonary artery pressure. The pulmonary artery pressure fell to 75% of systemic level in the immediate postoperative period and dropped below 50% after extubation. The prostaglandin infusion was withdrawn without elevation of pulmonary artery pressure on the second postoperative day. An echocardiogram performed on the second postoperative day showed good biventricular function with mild regurgitation of the tricuspid valve. There was no residual shunt across the patch and no gradient across either the left or right ventricular outflow tracts. The patient, at 3 months' follow-up, is alive and well with no change in echocardiographic features.

Comment

The association of AVSD with TGA is rare. In a large series of 400 hearts with TGA there was only one with AVSD [1]. In a review of 132 cases of TGA, 2 had an AVSD

Accepted for publication March 2, 1992.

Address reprint requests to Dr Kumar, King Faisal Specialist Hospital and Research Centre, MBC 16, PO Box 3354, Riyadh 11211, Saudi Arabia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

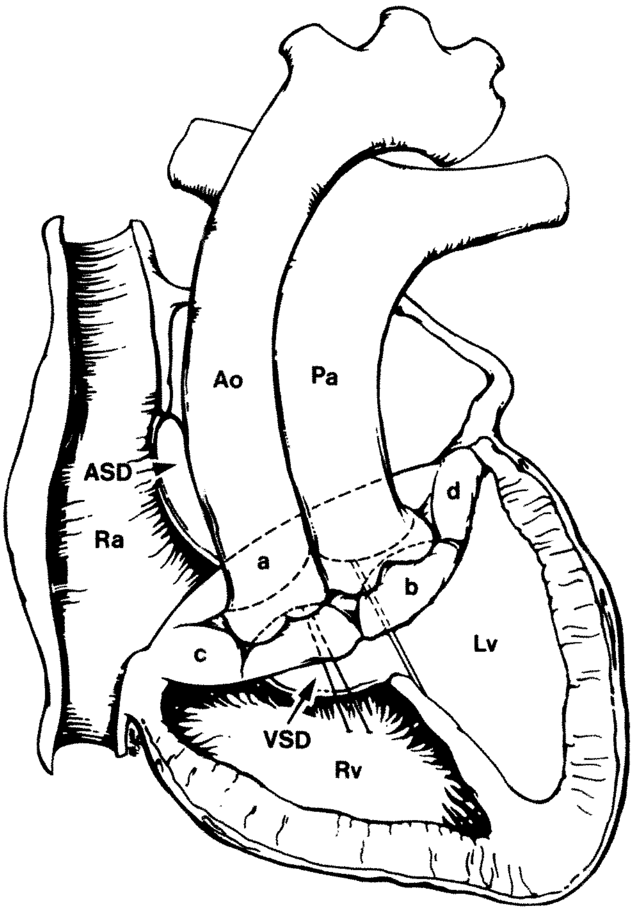


Fig 1. Schematic representation of transposition of the great arteries with atrioventricular canal. (a = *posterior leaflet;* Ao = *aorta;* ASD = *atrial septal defect;* b = *anterior leaflet;* c = *right lateral leaflet;* d = *left lateral leaflet;* LV = *left ventricle;* Pa = *pulmonary artery;* RA = *right atrium;* RV = *right ventricle;* VSD = *ventricular septal defect.)*

along with 1 case of AVSD, TGA, and patent ductus arteriosus (2.3%) [2]. In another large review of 507 specimens of hearts with AVSD, 17 were found to have complete TGA [3].

This anomaly is commonly reported with pulmonary atresia, or pulmonary valvular and subpulmonary stenosis [3]. In the same series the authors had reported only 1 case of an intermediate type where the anterior bridging leaflet was not free floating.

Surgical correction of this anomaly in hearts with pulmonary obstruction has been undertaken using a Rastelli [4] procedure or the Fontan principle [5]. Physiological correction using atrial redirection and AVSD repair has been carried out in 4 patients with AVSD associated with TGA by Pacifico and associates [6]. These authors repaired the defects using a modified Senning procedure in 2, modified Mustard operation in 1, and atrial baffle with ventricular inversion in 1. We performed total correction using both ventricles without a conduit.

The AVSD repair was carried out with two patches of bovine pericardium for closure of the defect without dividing the atrioventricular valve leaflets [7]. Only minimal suturing of the anterior and posterior leaflets of the mitral valve was necessary for its competence. The tricuspid valve was also similarly repaired. It is worth mentioning that the original pulmonary artery was three times the size of the aorta and considerable tailoring was needed for the anastomosis of great vessels to the new roots.

In view of the unrestricted pulmonary blood flow and systemic pulmonary artery pressure, the patient was prophylactically kept on prostaglandin infusion with continuous pulmonary artery pressure monitoring. Her pulmonary artery pressure stabilized at less than half systemic pressure with captopril therapy. As the patient did not have further elevation of pulmonary artery pressure, we believed that the pulmonary hypertension was reversible and would not be a problem in the long term. In this particular situation, the large ventricular component of the AVSD and the elevated pulmonary artery pressure almost certainly maintained left ventricular mass, which aided successful support of the systemic circulation after the arterial switch procedure.

We conclude that arterial switch with AVSD repair using both ventricles is feasible in anatomically favorable types of d-TGA with AVSD.

We thank Mr Jose Edgardo for the illustrations and Alison Silkstone for her secretarial assistance.

References

1. Shaher RM. Complete transposition of great vessels. New York: Academic Press, 1973:162.
2. Boesen IB. Complete transposition of the great vessels. Importance of septal defects and patent ductus arteriosus. Circulation 1963;28:885–7.
3. Bharati S, Kirklin JW, McAllister HA, Lev M. Surgical anatomy of common atrioventricular orifice associated with tetralogy of Fallot, double outlet right ventricle and complete regular transposition. Circulation 1980;61:1142–9.
4. McGoon DC, Wallace RB, Danielson GK. The Rastelli operation. Its indications and results. J Thorac Cardiovasc Surg 1973;65:65–75.
5. Gonzalez-Lavin L, Blair TC, Chi S, Sparrow AW. Orthoterminal correction of coexisting d-transposition of great arteries, subpulmonary stenosis and a complete form of atrioventricular canal. J Thorac Cardiovasc Surg 1977;73:694–8.
6. Pacifico AD, Ricchi A, Bargeron LM Jr, Colvin EC, Kirklin JW, Kirklin JK. Corrective repair of complete atrioventricular canal defects and major associated cardiac anomalies. Ann Thorac Surg 1988;46:645–51.
7. Pacifico AO, Kirklin JW, Bargeron LM Jr. Repair of complete atrioventricular canal associated with tetralogy of Fallot or double outlet right ventricle: Report of 10 patients. Ann Thorac Surg 1980;29:351–6.

New Surgical Technique for Total-Defect Aortopulmonary Window

Osamu Matsuki, MD, Toshikatsu Yagihara, MD, Fumio Yamamoto, MD,
Kyoichi Nishigaki, MD, Hideki Uemura, MD, and Yasunaru Kawashima, MD

Department of Cardiovascular Surgery, National Cardiovascular Center, Suita, Japan

A new technique is described to repair aortopulmonary window with total defect in an 8-day-old baby. Because we expected the future growth of aorta, we used the anterior wall of the pulmonary artery as a large flap to reconstruct the posterolateral aortic wall. An equine pericardial patch was used to repair the defect in the pulmonary artery. This is a logically effective method for aortic reconstruction in a neonate with a large aortopulmonary septal defect.

(Ann Thorac Surg 1992;54:991–2)

Aortopulmonary window is a rare anomaly, which usually needs to be surgically corrected relatively early in life to avoid the progress of pulmonary vascular disease. Considering the importance of the growth of aorta, a new surgical technique was applied successfully in a neonatal patient.

Material and Methods

Patient

A 7-day-old baby was seen at the National Cardiovascular Center with severe congestive heart failure. Echography suggested aortopulmonary window, coarctation of aorta, patent ductus arteriosus, small ventricular septal defect, and patent foramen ovale. Cardiac catheterization confirmed the existence of aortopulmonary window with a large aortopulmonary septal defect involving the entire length of the main pulmonary artery from immediately above the aortic and pulmonary valves to the ceiling of the pulmonary bifurcation. The pulmonary to systemic pressure ratio was 0.97 and the pulmonary to systemic flow ratio was 4.27. One-stage repair was performed on the eighth day after birth.

Surgical Technique

Through a median sternotomy, ordinary cardiopulmonary bypass was established with an additional arterial cannula in the descending aorta. The ascending aorta was cross-clamped and the heart was arrested with cold crystalloid cardioplegic solution. Under circulatory arrest, the patent ductus arteriosus was divided and the ductus arteriosus tissue was resected from the aorta followed by extended direct anastomosis. After bypass was restarted, as shown in Figure 1, the anterior wall of the pulmonary artery was widely opened to form a large, square flap, leaving the posterior wall of the pulmonary artery to keep the continuity of right and left pulmonary arteries as well as the pulmonary valve ring. The square flap was large enough to close the defect in the posterolateral aortic wall. Continuous suture with 7-0 Prolene (Ethicon, Somerville, NJ) was performed for this reconstruction. The ventricular septal defect, which was 4 mm in diameter and located in the muscular outlet portion, was closed directly through the pulmonary artery. After unclamping of the aorta, the anterior wall of the pulmonary artery was reconstructed using a glutaraldehyde-treated equine pericardial patch with 7-0 Prolene continuous suture.

The patient made an uneventful recovery, was extubated on the fifth postoperative day, and has been doing well for half a year.

Comment

There have been a number of reports [1–3] published concerning the operative method for aortopulmonary window. The spectrum of this anomaly is too wide [4] to choose only one method as an ideal one. When the defect is relatively small and its location is suitable, as reported by Kitagawa and associates [5], reconstruction of both aorta and pulmonary artery without any foreign material is a reasonable method.

When the defect is large, classified as "total defect" by Mori and co-workers [6], future stenosis of the reconstructed aorta should be avoided by using a large flap of pulmonary artery wall. Shatapathy and colleagues [7], in 1987, reported a method to use some part of pulmonary artery for the reconstruction of aorta, which was applied to an 18-year-old patient. They stressed the easiness and security of the procedure itself. Our method is different from theirs because it was applied to a neonate with a large defect. Prompting the natural growth of aorta is the main aim of our choice of this new method. Because the

---

Accepted for publication June 30, 1992.

Address reprint requests to Dr Matsuki, Department of Cardiovascular Surgery, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita, 565 Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

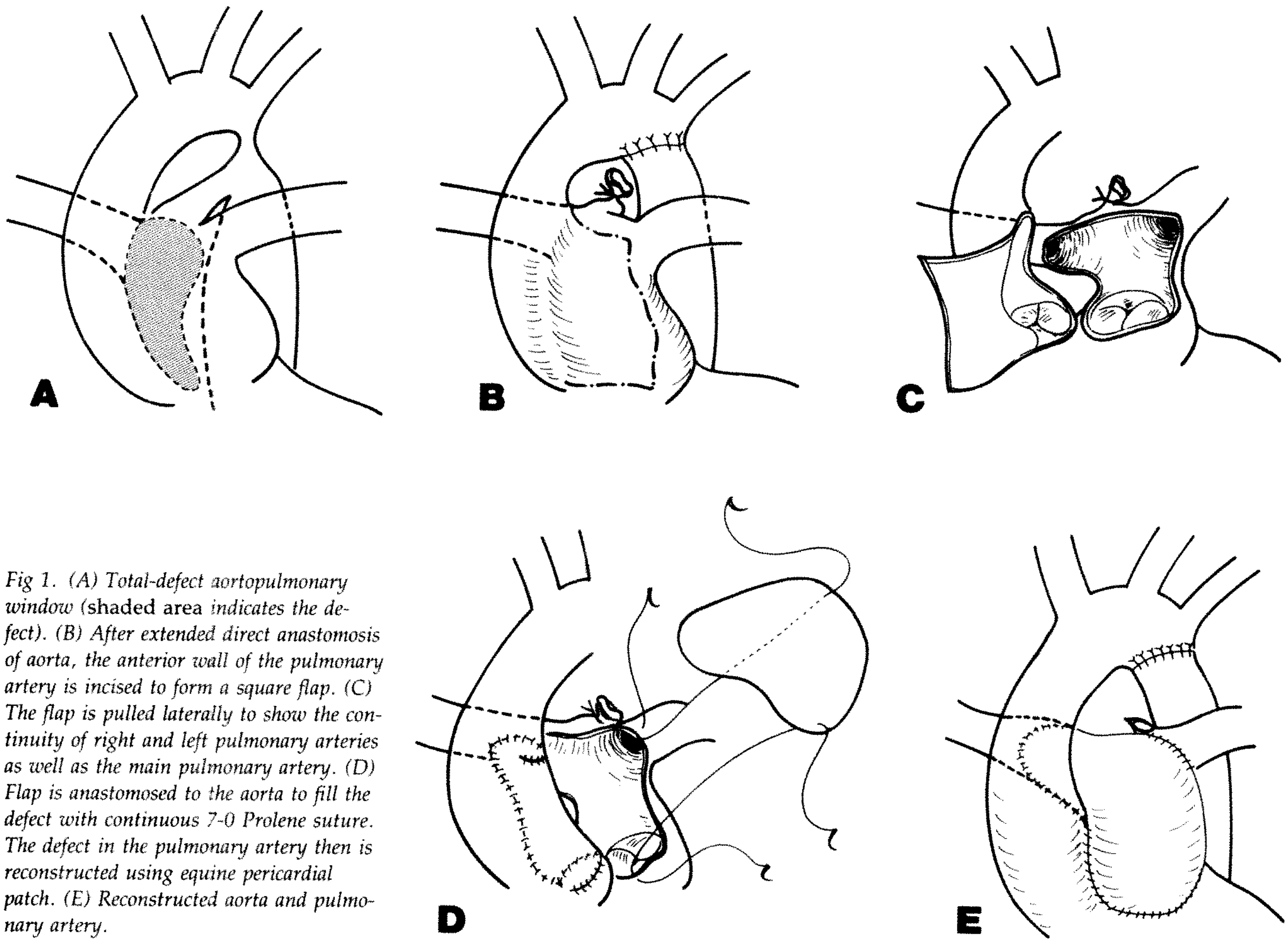


*Fig 1. (A) Total-defect aortopulmonary window (*shaded area *indicates the defect). (B) After extended direct anastomosis of aorta, the anterior wall of the pulmonary artery is incised to form a square flap. (C) The flap is pulled laterally to show the continuity of right and left pulmonary arteries as well as the main pulmonary artery. (D) Flap is anastomosed to the aorta to fill the defect with continuous 7-0 Prolene suture. The defect in the pulmonary artery then is reconstructed using equine pericardial patch. (E) Reconstructed aorta and pulmonary artery.*

defect of the pulmonary artery that was closed by xenograft pericardium is relatively large, careful follow-up is mandatory, but our new method is logically ideal as a choice for a small infant with a large defect.

References

1. Clarke CP, Richardson JP. The management of aortopulmonary window: advantages of transaortic closure with a Dacron patch. J Thorac Cardiovasc Surg 1976;72:48–51.
2. Doty DB, Richardson JV, Falkovsky GE, Gordonova MI, Burakovsky VI. Aortopulmonary septal defect: hemodynamics, angiography, and operation. Ann Thorac Surg 1981;32:244–50.
3. Ravikumar E, Whight CM, Hawker RE, Celermajer JM, Nunn G, Cartmill TB. The surgical management of aortopulmonary window using the anterior sandwich patch closure technique. J Cardiovasc Surg (Torino) 1988;29:629–32.
4. Richardson JV, Doty DB, Rossi NP, Ehrenhaft JL. The spectrum of anomalies of aortopulmonary septation. J Thorac Cardiovasc Surg 1979;78:21–7.
5. Kitagawa T, Katoh I, Taki H, et al. New operative method for distal aortopulmonary septal defect. Ann Thorac Surg 1991;51:680–2.
6. Mori K, Ando M, Takao A, Ishizawa S, Imai Y. Distal type of aortopulmonary window: report of 4 cases. Br Heart J 1978;40:681–9.
7. Shatapathy P, Rao KM, Krishnan KV. Closure of aortopulmonary septal defect. J Thorac Cardiovasc Surg 1987;93:789–91.

Newly Developed Holder for a Right-Angled Metal Venous Cannula

Takashi Watanabe, MD, Toshio Abe, MD, Minoru Tanaka, MD, Kenzo Yasuura, MD, Hiroshi Hikosaka, MD, Yoshito Suenaga, MD, and Hidekazu Hosokawa, MD

Department of Thoracic Surgery, Nagoya University School of Medicine, and Division of Cardiovascular Surgery, Nagoya Daini Red Cross Hospital, Nagoya, Japan

A newly developed holder for a right-angled metal venous cannula was developed to make direct insertion into each cava easier, especially insertion into the superior vena cava in pediatric open heart operations. We have been using this holder with ease and safety in all cases of small babies.

(Ann Thorac Surg 1992;54:993–4)

In pediatric open heart operations, a right-angled metal cannula for direct vena caval cannulation (Pacifico's venous cannula; DLP Inc, Grand Rapids, MI) is frequently used to maintain good venous drainage and good exposure of the right atrium [1]. Although insertion into the inferior vena cava is relatively easy, it is often difficult to insert the cannula into the superior vena cava, especially that of small babies or infants. Beginners in cardiovascular surgery who are not accustomed to this cannula may often have difficulty in doing it, which can be a cause of

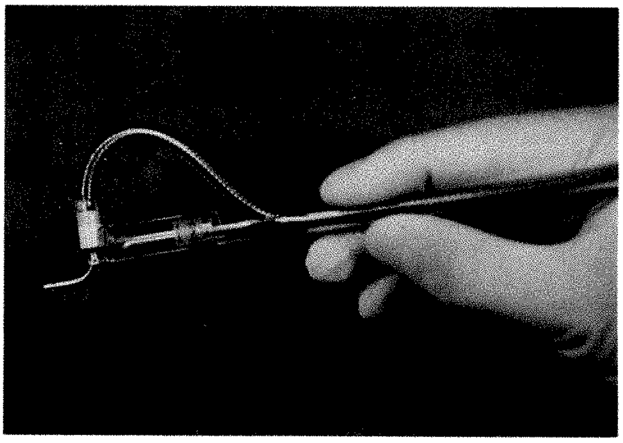


Fig 1. The right-angled metal venous cannula is attached to a newly developed holder. The holder is made of polyvinyl chloride and can make a straight line from the metal tip to the flexible plastic tube after arch formation.

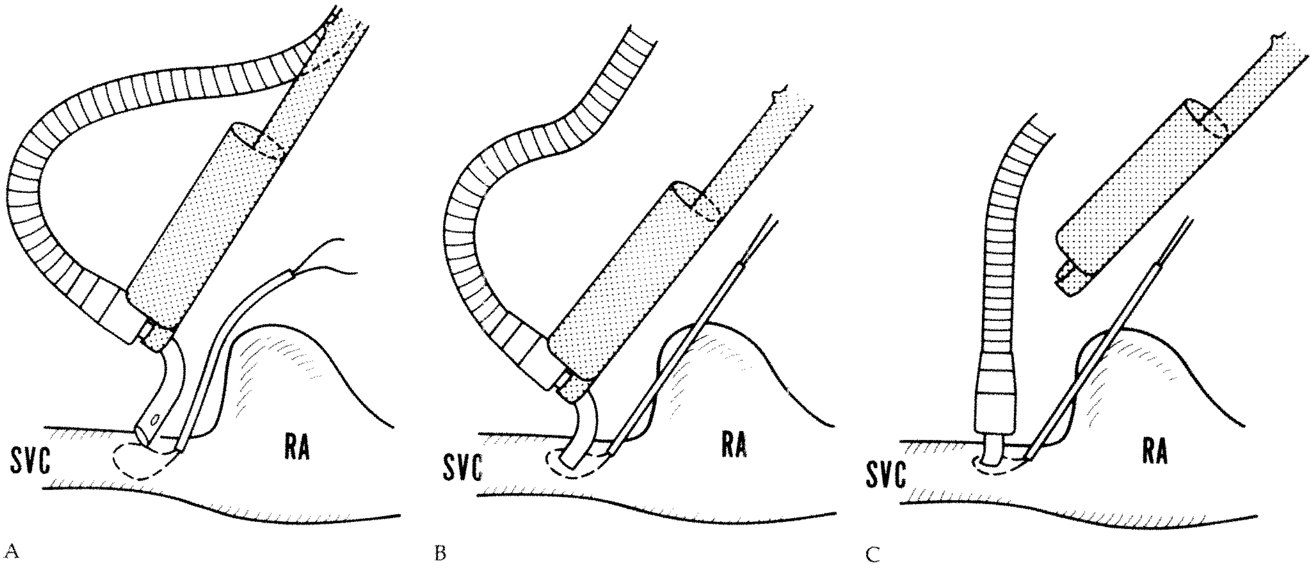


Fig 2. Insertion of the right-angled metal cannula into the superior vena cava (SVC) with the holder. The operator can make the insertion in the usual manner for cannulation. (RA = right atrium.)

Accepted for publication July 15, 1992.

Address reprint requests to Dr Watanabe, Department of Thoracic Surgery, Nagoya University School of Medicine, 65 Tsurumai-Cho, Showa-Ku, Nagoya 466, Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

bleeding around the insertion site. We developed a holder to resolve this problem.

The right-angled metal venous cannula is attached to the polyvinyl chloride holder, which makes a straight line from the metal tip to the flexible plastic tube after arch formation (Fig 1). As for a usual venous cannulation, it is held in the right hand of an operator and its metal tip is inserted into the superior vena cava directly through a small incision (Fig 2). A pursestring suture around the incision with a tourniquet is tightened by an assistant, and the holder is released. We have been using this holder with ease and safety in all pediatric open heart operations for small babies.

Reference

1. Kirklin JW, Barratt-Boyes BG. Clinical methodology of cardiopulmonary bypass. In: Kirklin JW, Barratt-Boyes BG, eds. Cardiac surgery. New York: Wiley, 1985:59.

REVIEW OF RECENT BOOKS

A Textbook of Cardioplegia for Difficult Clinical Problems

Edited by Richard M. Engelman, MD, and Sidney Levitsky, MD
Mount Kisco, NY, Futura, 1992
334 pp, illustrated, $75.00

Reviewed by Edward Y. Sako, MD, PhD

An international group of contributors have been assembled in a book that addresses not only cardioplegia but the general field of myocardial protection in a variety of clinical situations. The two editors are both well-known cardiac surgeons with a great deal of experience in this field. As noted in the preface, many of the topics were presented at the International Conference on Cardioplegia held in Oxford, England, in August 1990.

The book begins with chapters outlining the historical development of myocardial protection both in the United States and in Europe. Although brief, they give some perspective to the book and highlight many of the pioneers in the field. The book then moves on to specific clinical problems.

Topics covered include aortic regurgitation, percutaneous transluminal coronary angioplasty (PTCA) failure, reoperations for coronary artery disease, methodologies employed for the dysfunctional or impaired ventricle, various valve operations, acute myocardial infarction, cardiac arrhythmia surgery, transplantation, and pediatric heart surgery. Many of the topics are presented in a duplicate fashion. For example, there are two chapters entitled "Cardioplegia for PTCA failure" and two chapters entitled "Cardioplegia for the dysfunctional ventricle." This allows the reader to compare different approaches to a given problem.

The individual chapters themselves are fairly succinct, averaging 10 to 15 pages each. Although some contain discussions of theoretical considerations and experimental studies, the majority of time is spent on practical clinical application. The techniques discussed include use of retrograde cardioplegia, blood versus crystalloid cardioplegia, substance-enhanced solutions, and warm continuous administration. Among the various chapters there is often overlap, repetition, and in some cases contradiction. This is to be expected given the variety of authors and the controversial nature of this field. The value of the book lies in the presentation of the specific protocol used by each author in the given clinical situations.

This book is an excellent reference and update on the latest methods of myocardial preservation. It should prove to be of value to any practicing cardiac surgeon.

San Antonio, Texas

Modified Urinary Collecting Bags for Prolonged Underwater Chest Drainage

Yaron Bar-El, MD, Yair Lieberman, MD, and Alon Yellin, MD

Departments of Cardiac and Thoracic Surgery, The Chaim Sheba Medical Center, Tel Hashomer, Israel

We describe a method by which a modified urinary collecting bag is used as part of a chest drainage system. This system is especially suitable for patients who require prolonged periods of drainage.

(Ann Thorac Surg 1992;54:995–6)

Patients who require pleural drainage after thoracic operations or for air leak, persistent effusion, or empyema are usually managed by a pleural tube connected to an underwater sealed collecting device. This arrangement is quite cumbersome for the patient who needs prolonged pleural drainage and who is ambulated and free to walk. We propose an effective and inexpensive yet simple, convenient, and lightweight drainage system for such patients.

Method

A simple polyethylene urine collecting bag is used. The bag is modified in such a way that a water seal is created within the bag. This is achieved by soldering the bag (with a soldering device used for closing polyethylene bags) so that an inflow tunnel is created, draining into the lower part of the bag, which contains a small amount of water (Fig 1). The tunnel is seen between the two vertical lines. During deep inspiration, the two sides of the bag in the central tunnel tend to adhere to each other, thus serving as a flutter valve further preventing reflux into the chest tube. When there is excessive air leak, a small hole is made in the upper part of the bag, allowing the air to escape.

Use of this bag, especially if attached to the patient's garments, allows convenient mobilization and free use of the hands (Fig 2). The inexpensive bag is replaced daily.

We have used this drainage method on 6 patients with empyema (2 postoperative, 1 traumatic, 3 parapneumonic), 2 with bronchopleural fistula, 1 with prolonged air leak after segmentectomy, and 3 elderly patients with pneumothorax associated with emphysema. The system was used for 7 to 30 days (mean, 18 days). All but 2 patients were discharged and continued treatment as outpatients. There were no complications related to the technique.

Comment

A catheter or tube is usually left in the pleural space after open and closed thoracotomy procedures to drain fluid and air, and to allow the lung to expand. To prevent air and fluid reflux, either a molded plastic apparatus with a water seal or a one-way flutter valve (Heimlich valve) is used [1]. These two commonly used methods have their shortcomings. The underwater sealed apparatus is usually cumbersome, heavy, and inconvenient, especially for the ambulated patient who may require a longer period of

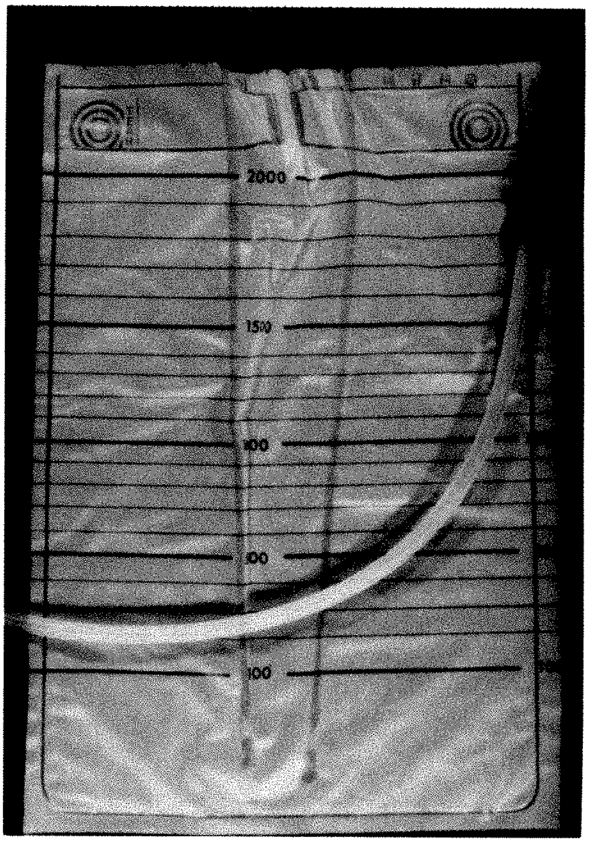


Fig 1. The modified urinary collecting bags. Note the two soldering lines beginning at the top of the bag and continuing almost to the bottom.

Accepted for publication July 27, 1992.

Address reprint requests to Dr Yellin, Department of Thoracic Surgery, The Chaim Sheba Medical Center, Tel Hashomer 52621, Israel.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

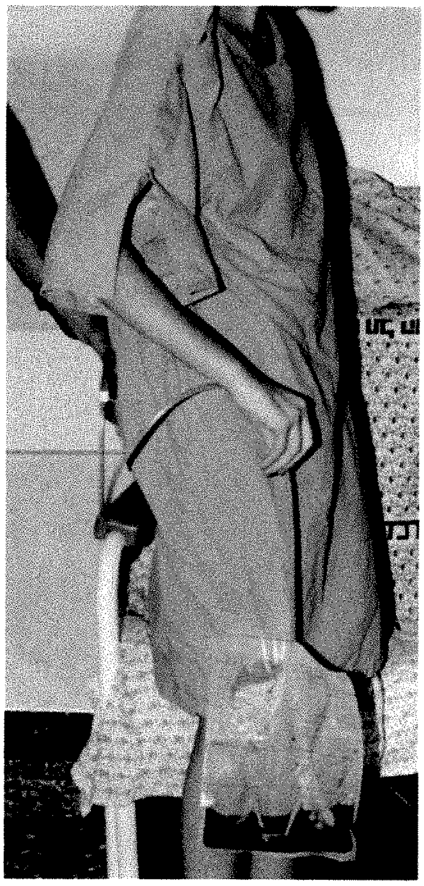


Fig 2. The collecting system in use.

pleural drainage. The rigid apparatus usually needs some support mechanism to remain in the upright position. The Heimlich flutter valve, on the other hand, is light and convenient, but blood or other thick pleural fluids that pass between its two rubber leaves may cause them to adhere to each other, thus obstructing the lumen and preventing further drainage.

Our proposed system overcomes the disadvantages of both methods. The lightweight bag is convenient for use and can be carried either on or under the garments. During sleep it can be attached to the bed. The walls of the bag, in a fashion similar to the Heimlich device, act as a flutter valve but are less liable to cling to each other, thereby allowing the bag to remain patent. In addition, this system is obviously cost-saving, requiring only inexpensive urinary collecting bags modified with a simple soldering device. Because active suction (negative pressure) cannot be applied to the bag, its use is not recommended in the immediate postoperative period. However, we do find it applicable for those patients who require prolonged pleural drainage, and especially for those who are ambulatory or can be discharged from the hospital. Although not yet tested, this system might also be suitable in emergency situations (eg, military, trauma) when immediate intrapleural drainage is required.

Reference

1. Heimlich HJ. Valve drainage of the pleural cavity. Dis Chest 1968;53:282–7.

Clarence Crafoord and the First Successful Resection of a Cardiac Myxoma

W. Randolph Chitwood, Jr, MD

Division of Cardiothoracic Surgery, East Carolina University School of Medicine, Greenville, North Carolina

In 1954 Clarence Crafoord, the pioneer Swedish cardiovascular surgeon, removed an intraatrial myxoma for the first time. The patient was a 40-year-old woman with atypical symptoms of mitral stenosis. Follow-up 38 years later finds the patient alive and well. This case represents not only the first extirpation of a cardiac tumor on cardiopulmonary support but also the dawn of open cardiac surgery in Sweden. Others were soon to follow the lead of Crafoord and his team. However, their bold efforts prepared the way for the early diagnosis and facile extirpation of cardiac myxomas. Moreover, this group played an integral part in the development of safe, effective cardiopulmonary perfusion.

(Ann Thorac Surg 1992;54:997–8)

Although the first cardiac neoplasm was described in 1559 by Realdo Colombo [1], Vesalius' successor at Padua, a successful surgical removal was not to occur for almost 400 years. Few early attempts were made to remove cardiac neoplasms. Without the advantages of cardiopulmonary bypass, Beck and Maurer resected a right ventricular teratoma in 1936 and left ventricular lipoma in 1951, respectively [2, 3]. In 1952, Bahnson and Newman [4] prolapsed a large myxoma through a right atriotomy under inflow occlusion and successfully excised the mass. Unfortunately, the patient died unexpectedly 24 days after the procedure.

The Swedish pioneer cardiovascular surgeon, Clarence Crafoord, perhaps is best known for the first resection of an aortic coarctation in 1944. However, modern cardiac surgeons may be interested that in 1954, during the first Henry Ford International Symposium of Cardiovascular Surgery in Detroit, he reported the first successful removal of an atrial myxoma [5]. Many other seminal presentations were delivered during that conference, and transactions of the meeting remain a standard reference in the history of cardiac surgery. Robert Glover of Philadelphia presented 750 cases of digital commisurotomy for mitral stenosis. Among the six discussants of Glover's paper was Crafoord, who limited his discussion to a most unusual form of mitral obstruction: a left atrial myxoma [5].

In July of 1954 a 40-year-old woman had been referred to Professor Crafoord as having an atypical case of mitral stenosis; she had dizziness and transient hemiparesis but had a sinus rhythm. A direct atrial puncture with pressure measurements and radiographic contrast injections were made to determine the diagnosis. The angiogram was the only illustration published in his brief description of the procedure. Crafoord stated simply [5]:

> She was on extracorporeal complete circulation and oxygenation for thirty minutes during the time of intervention, when we opened up the left atrium very widely and during which time we compressed the mitral orifice.
>
> I had my assistant compress the left ventricle so that it completely closed from the time the artificial circulation was started. Then I opened up the atrium, and it was possible to remove this huge tumor practically in one piece. Some of it could not be taken out of the incision, although the incision was very large. It had to be broken up in three different parts. . . . A little less than one year after the operation she is in very good condition.

Additional details of the operation and extended patient follow-up never were published by Crafoord. In recent communications Professors Åke Senning and Viking Björk recounted many details of this classic case for me. The diagnostic angiogram was done by Drs Björk and Nordenström, and recently Björk described the conduct of that study as follows (Björk VO, personal communication, June 1992):

> In 1952 the new angiographic machine had been installed at the Children's Clinic of the Karolinska Hospital where Kjellberg and Rudhe worked. I had developed the complete left heart catheterization by introducing an 18-cm-long needle above the ninth right rib, three finger breadths to the right of the midline on the back of the patient, the needle touching the vertebral body, advancing into the left atrium. The cardiologist, Nordenström, and I took the patient in our car [from Sabbatsberg's sjukhus (ie, hospital), Stockholm] at 7 in the morning, where I introduced the needle and the contrast. As the posterior wall of the left atrium was free from tumor . . . we got a very sharp picture of the myxoma, fixated by a root to the membranous portion of the atrial septum, and in each diastole moving down and obstructing the mitral orifice. The patient had sinus rhythm, so from this case we learned that when we found a very tight mitral stenosis in sinus rhythm, we suspected a left atrial myxoma.

Dr Senning joined Professor Crafoord at Sabbatsberg's Hospital in 1948 and with P. A. Astradsson, an engineer, was given the task of constructing a pump-oxygenator. They were not to move to the Karolinska Institute until 1957. John Gibbon came to Stockholm and helped them

---

Address reprint requests to Dr Chitwood, Department of Surgery, East Carolina University School of Medicine, Greenville, NC 27858.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

with their third surviving animal experiment. After liaison with Gibbon, Kirklin, Bigelow, Harken, and Dennis in the United States, Senning's team developed an extracorporeal perfusion system in Stockholm. However, they determined experimentally that their system probably would not be suitable for normothermic human perfusion. Thereafter, they settled on a combination of perfusion hypothermia, decreased flow, and ventricular fibrillation (to prevent air embolism) as the initial method for clinical extracorporeal support [6].

Extracorporeal circulation was used for the first time in Sweden during Crafoord's excision of the myxoma [6]. Senning assisted Professor Crafoord, along with Liedström, Wiklund, and Björk. Recently, Professor Senning recounted this pioneering operation as follows (Senning A, personal correspondence, June 1992):

> The patient was anesthetized and made hypothermic, 30°C, with surface cooling in a temporary "tub" [viz, wooden walls] on the operation table. I had given her 5 gr of alcohol intravenously to dilate the periphery to expedite the temperature drop. At 30°C the temporary bathtub was removed and the [heart-lung] machine connected. She was then further cooled to 28°C with the machine.
>
> Crafoord had insisted on a left-sided thoracotomy, which made an exploration of the septum difficult, but allowed a large atriotomy from the atrial appendix into the upper left pulmonary vein. Ventricular fibrillation was electrically induced, the atrium was opened and the tumor prolapsed into the incision. It was thought too large and was divided in three pieces, as Crafoord mentioned. The blood was aspirated and the atrium carefully inspected, and the atrium and mitral area were carefully flushed.
>
> The atriotomy was sutured, but just before it was completely closed the heart defibrillated spontaneously—a situation I had never seen in some hundred dog experiments. Being the first assistant, I immediately compressed the left ventricle to avoid a diastolic dilation of the ventricle—as I used to do in the lab before I introduced the ventricular fibrillation. A few seconds later the incision was closed. The rewarming to 29°C was started with the machine. After a careful hemostasis, the thoracotomy was closed, and the patient was rewarmed in the "tub" to 36.9°C. During the rewarming an [intraarterial] blood pressure was continuously monitored and electrocardiogram intermittently. She had a sudden blood pressure drop of 1 to 2 minutes to 35 to 40 mm Hg. I believed it was a short period of ventricular fibrillation, but it stopped before I could register it.
>
> As we were afraid of further such complications, we left the patient on the operation table until the next morning and I rested on a stretcher next to her. She was sent to the ward fully awake, and her hospital stay was uncomplicated and she left for home very happy.
>
> I just phoned her and she is, *'mår alldeles utmärkt'*—that means she feels very fine—38 years postoperatively.

This classic vignette in cardiac surgery illustrates the innovative spirit of Crafoord, Senning, Björk, Nordenström, and others in Stockholm during those early days of cardiac surgery. Moreover, this particular operation serves not only as a landmark in extirpative technique, but also as a milestone in extracorporeal support. As Senning stated recently (Senning A, personal correspondence, June 1992):

> To me it was a happy moment to see that the technique I worked out in the dog lab, [extracorporeal circulation] combined with hypothermia and cardiac "standstill" with electrically induced ventricular fibrillation, worked even clinically in spite of the very traumatizing oxygenator.

An appropriate tribute to Crafoord and his associates remains the relative ease and safety with which we are able to diagnose and treat patients with cardiac myxomas today. However, some benign and all malignant cardiac neoplasms continue to be a serious operative challenge for us today.

Addendum

On September 9, 1992, Dr Senning wrote me a second follow-up letter, which said:

> Two months ago I met Mrs B, our first patient of 14 August 1954 . . . an 82-year-old lady in excellent cerebral and physical condition, with all 32 teeth intact . . . coquett[ish] and fashionably well dressed. She remembered, she was freezing and shivering waking up . . . but was grateful for the extra 40 years.

I thank Professors Senning and Björk for their first-hand and insightful descriptions of this classic case.

References

1. Colombo R. De re anatomica. Venice: Nicolai Benilacquae, 1559.
2. Beck CS. An intrapericardial teratoma and tumor of the heart: both removed operatively. Ann Surg 1942;116:116–74.
3. Mauer ER. Successful removal of a tumor of the heart. J Thorac Surg 1952;3:479–82.
4. Bahnson HT, Newman EV. Diagnosis and surgical removal of intracavitary myxoma of the right atrium. Bull Johns Hopkins Hosp 1953;93:150–63.
5. Crafoord C. Discussion of Glover RP. The technique of mitral commisurotomy. In: Lam CR, ed. Henry Ford Hospital: International Symposium on Cardiovascular Surgery. Philadelphia: Saunders, 1955:202–3.
6. Senning A. Developments in cardiac surgery in Stockholm during the mid and late 1950s. J Thorac Cardiovasc Surg 1989;98:825–32.

Surgical Treatment for Higher Stage Non–Small Cell Lung Cancer

Dirk E. Van Raemdonck, MD, Airton Schneider, MD, and Robert J. Ginsberg, MD

Sloan-Kettering Institute; Department of Thoracic Surgery, Memorial Sloan-Kettering Cancer Center; and Department of Surgery, Cornell University Medical College, New York, New York

Locally advanced lung cancer (stage IIIa, IIIb) in which the primary tumor is proximal (T3) or has invaded adjacent structures (T3) or organs (T4) or in which mediastinal lymph nodes are involved (N2, N3) worsens the prognosis significantly. However, in stage IIIa (T3 or N2), when surgical treatment results in total removal of the primary tumor and involved lymph nodes, there still is a reasonable chance for ultimate cure. On the other hand, total excision can be very rarely performed in T4 or N3 tumors. Therefore, this group (stage IIIb) usually indicates unresectability. Disseminated lung cancer with distant metastasis (stage IV) is still considered to be incurable. Nevertheless, solitary metastatic sites (M1), especially brain, have been treated on occasion by resection of the primary tumor and removal of the solitary metastasis. This appears to improve median survival and does yield 5-year survival in selected patients. The results after surgical treatment in these patients with higher stage lung cancer reported over the last 10 years are reviewed.

(Ann Thorac Surg 1992;54:999–1013)

The most recent statistics reveal the number of new lung cancer cases per year in the United States to be 161,000 [1], of which approximately 80% [2] or 128,800 will be non–small cell lung cancers (NSCLCs).

The prognosis in patients with NSCLC remains very dismal, with an overall 5-year survival at the time of diagnosis approximating 14% [3]. There is no doubt that survival at 5 years is closely related to the stage of the disease at the time of presentation and that surgical resection offers the best chance for ultimate cure [4] (Table 1).

In the medical community, there is general agreement that definitive surgical treatment is the first choice of therapy for all patients with NSCLC limited to the lung, whether intrapulmonary nodes are involved or not (stages I and II). Five-year survivals after surgical resection in these early stages of NSCLC are reported as high as 70% and 50%, respectively [4]. Radiotherapy alone with curative intent (6,000 cGy), administered for medical reasons or because the patient refused operation [5, 6] or as an alternative to operation in elderly (>80 years) patients with an increased operative morbidity and mortality [7], will yield long-term survival in these patients with early stage NSCLC in only 15% to 20%.

More than half of all patients with NSCLC will have extrapulmonary or extrathoracic spread of their lung cancer (stages III and IV) when first seen [8]. Considerable differences of opinion exist regarding operation versus other treatment modalities for these patients with higher stage lung cancer.

For this review, we analyzed the results reported in the Anglo-American literature between 1980 and 1991 after surgical treatment in advanced NSCLC (stages III and IV). Only articles using the new TNM staging system [8] or articles reporting results according to the old TNM [9] or other staging systems [10] comparable with a concordant category in the new TNM staging were selected. In the tables, we only refer to the most updated report from any single institution. Articles reporting results in fewer than 10 patients were also excluded, unless no other series was available in a specific TNM or stage subgroup.

Although the new staging system [8] has provided a high level of consistency in classification with minimal variability among physicians throughout the world, there is still a great diversity in the method of reporting survival results. Survival rates from surgical as well as other treatment series can be greatly modified by selection of patients at the time of evaluating survival data. Surgical cure rates can be determined from the total number of patients with the disease, the total number accepted for operation, or the number "completely" resected, with or without exclusion of operative mortality. It is obvious that the smaller the denominator from which the patients are derived, the better the reported results will be. Patient selection makes comparison of series between different institutions quite difficult and continues to contribute to the wide range in reported 5-year survival rates. We agree with Watanabe and associates [11] that there is a strong need for international standardization in reporting survival rates. Completeness of resection also has been divergently defined by different authors, varying from resection of the primary tumor together with all accessible mediastinal lymph nodes [11], to the preceding plus microscopic negative margins and no gross disease left behind [12], to all of the preceding plus the most distal node free of tumor and no perinodal extension [13].

Address reprint requests to Dr Ginsberg, Thoracic Service, Department of Surgery, Memorial Sloan-Kettering Cancer Cencer, 1275 York Ave, New York, NY 10021.

© 1992 by The Society of Thoracic Surgeons 0003-4975/92/$5.00

Table 1. Prognosis of 1,737[a] Patients After Resection of Lung Cancer According to the Postoperative TNM Classification

Stage	TNM	No. of Patients	Five-Year Survival Rate (%)
I	T1 N0 M0	245	75.5
	T2 N0 M0	291	57.0
II	T1 N1 M0	66	52.5
	T2 N1 M0	153	38.4
IIIa	T3 N0 M0	106	33.3
	T3 N1 M0	85	39.0
	T1–3 N2 M0	368	15.1
IIIb	T1–3 N3 M0	55	0
	T4 any N M0	104	8.2
IV	any T any N M1	258	7.5

[a] 3.3% small cell carcinoma included.

Adapted from Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. J Thorac Cardiovasc Surg 1988;96:440–7.

Staging

Stage IIIa

Stage IIIa is defined to include patients with a potentially resectable T3 lesion as well as those with N2 disease [8]. The largest retrospective series reporting on survival after operation in these patients was published in 1988 by Naruke and co-workers [14]. During a 25-year period, 559 patients underwent resection for a T3 or an N2 lesion with an actuarial 5-year survival of 22.2%. In 1990, Mountain [15] reported a 5-year survival rate of 28% in a selected group of 198 completely resected patients, excluding an operative mortality of 6.7%.

The widely accepted new TNM staging system for lung cancer [8] has already proved to be a useful classification for grouping patients with similar prognoses and therapeutic options [16]. Nevertheless in stage IIIa, as further demonstrated in this review, there is a great difference in prognosis between patients with T3 N0–1 disease and patients with any T N2 disease, as the outcome in the former will not be much different from the T1–2 N0–1 group, once the tumor has been completely resected and locally controlled. Stage IIIa is not a homogeneous group with regard to prognosis.

T3 Tumors

Tumors invading the chest wall, the superior sulcus of the chest, the diaphragm, the mediastinal pleura, or the pericardium or a tumor within 2 cm of the carina are all classified as T3 lesions. Naruke and co-workers [14] reported an overall 5-year survival of 25.8% in 327 patients treated operatively for such a lesion. If mediastinal lymph nodes were free of disease, results were 31.6% and 33.7% for T3 N0 and T3 N1 disease, respectively. In 80 patients with a completely resected T3 N0–1 lesion, Mountain [15] reported a survival of 39%.

CHEST WALL INVASION. Peripheral tumors are often adherent to the parietal pleura as a result of concomitant infection and fibrosis. These can usually be separated from the chest wall by simple lysis of adhesions or extrapleural dissection. However, when such lesions have invaded the parietal pleura, the intercostal muscles, or even the ribs (T3), more extensive operation, often including chest wall reconstruction, will be required to achieve complete resection.

The overall 5-year survival in patients with a surgically resected tumor invading the chest wall ranged from 12% to 40% [15, 17–25] (Table 2). Three major factors have been identified that adversely influence the prognosis in these patients. Nodal status was the most important prognostic factor in all reported series. In patients with N2 disease, although not common in these peripheral lesions, there were virtually no 5-year survivors. If lymph nodes were free of disease and a complete resection was performed, 5-year survival exceeded 50% [19–24]. Prognosis was also related to the completeness of resection, with no patient surviving 5 years after an incomplete resection [18, 19, 21, 24]. As well, survival appears significantly related to the depth of chest wall involvement [21]. Many authors believe that the use of en bloc chest wall resection (versus extrapleural dissection) should be advocated for all lesions invading the parietal pleura. A recent study reported that the length of pleural involvement adversely affected survival [24].

The role of adjuvant radiotherapy for these lesions remains unclear. Although the Toronto experience suggested that adjuvant radiotherapy may prolong survival [19], its use is usually reserved for patients with incomplete resection or involved mediastinal lymph nodes. The Lung Cancer Study Group (LCSG) attempted to conduct a randomized comparative trial evaluating the role of postoperative radiation therapy after complete resection of a bronchogenic carcinoma involving the chest wall (LCSG 841). However, low accrual forced abandonment of the trial. In one retrospective analysis, the use of preoperative radiotherapy appeared to improve survival [23].

SUPERIOR SULCUS TUMORS. A tumor at the apex of the lung can invade through the parietal pleura into the upper ribs, the brachial plexus and subclavian vessels, the sympathetic chain, including the stellate ganglion (T3), or vertebral body (T4), causing the Pancoast syndrome.

Table 2. Reported Results After Surgical Treatment for NSCLC With Chest Wall Invasion (T3)

First Author [Reference]	No. of Cases Operated (CR)	Est. 5-Year Survival (%)	Mortality (%)
Paone [18]	32 (28)	35	3
Patterson [19]	35 (30)	38	9
Piehler [20]	93 (66)	33[a]	15
McCaughan [21]	125 (77)	40[a]	4
Van de Wal [22]	16 (NS)	12	6
Allen [25]	52 (NS)	26	4

[a] Survival after completely resection.

CR = complete response; NS = not stated.

Table 3. Reported Results After Surgical Treatment for NSCLC With a Superior Sulcus Lesion (T3)

First Author [Reference]	No. of Cases Operated	Est. 5-Year Survival (%)	Mortality (%)
Paulson [27]	79	31	3
Anderson [28]	28	34	7
Devine [29]	40	10	8
Rice [31]	36	28	0
Miller [34]	36	31	NS
McKneally [35]	25	51	NS
Ricci [37]	41	34	5
Carrel [23]	37	29	NS
Dartevelle [38]	24	32 (2 y)	4
Komaki [39]	25	40	NS

NS = not stated.

The overall 5-year survival for patients with resected tumors invading the superior sulcus of the chest has been reported in the range of 30% [15, 23, 26–39] (Table 3). Several adverse prognostic factors have been identified by different authors. The absence of involved mediastinal lymph nodes was again the most important prognostic factor, with 5-year survival as high as 50% in patients with a T3 N0 lesion and with only few long-term survivors in the N2 group [23, 27, 36]. Martini [4] pointed out that the finding of an isolated ipsilateral supraclavicular lymph node (N3), present in about 17% of his patients, did not interfere with complete resection and may not be a contraindication for operation. Adenocarcinoma on histologic examination, the presence of a Horner's syndrome, and bony erosion also appear to adversely influence prognosis.

Preoperative radiotherapy (30 to 40 Gy in 4 weeks to a portal that includes the primary tumor, the mediastinum, and the supraclavicular region) has been widely used since Paulson [27] in 1961 reported encouraging results in these tumors with a complete resection rate after radiotherapy of nearly 90%. Although its value has never been proved in a prospective randomized study, two retrospective analyses found a significant survival advantage in patients irradiated preoperatively [23, 36]. In the largest series, involving 129 patients operated on for a superior sulcus tumor at Memorial Sloan-Kettering Cancer Center, 5-year survival in patients treated in this way was 29% compared with 20% if no radiotherapy was administered preoperatively [36]. The use of postoperative radiotherapy, whether by interstitial implantation of radioisotopes (brachytherapy) or external beam, has been advocated in patients with incomplete resections to obtain local control [32, 35, 36]. Surprisingly, 14% to even 50% of these patients with "incomplete resections" treated in this way did experience prolonged survival [32, 36].

Invasion of the vertebral body (T4) or major neurovascular structures at the apex of the lung (T3) has usually indicated incurability of such a lesion. Dartevelle and associates [38], however, reported a 2-year survival rate of 32% in such a group of 24 patients using a combined cervical and thoracic approach with an operative mortality rate of 4.1%.

INVASION OF MEDIASTINAL PLEURA, PERICARDIUM, AND DIAPHRAGM. Local invasion of the mediastinal pleura, the pericardium, and the diaphragm has been defined as T3 disease [8]. However, invasion of the ipsilateral pulmonary artery and veins, often completely resectable by intrapericardial dissection, is not clearly described in the new staging system. Also, the presence of a pericardial effusion in these central tumors is not specified.

Very few series have reported results in patients with local invasion limited to the mediastinal pleura, pericardium, or pulmonary vessels [15, 40–42], and no isolated reports are available in which diaphragmatic invasion required resection. At Memorial Sloan-Kettering Center, of 225 patients who underwent thoracotomy for a primary NSCLC with mediastinal invasion (T3 to T4), 37% had involvement of the pulmonary artery, 25% of the pericardium, 23% of the pulmonary vein, 13% of the phrenic nerve, 9% of unspecified structures including isolated mediastinal pleural invasion, and 6% of the recurrent laryngeal nerve [40]. The perioperative mortality was 2.7%. The overall 5-year survival rate was 7% and 11%, 7%, 7%, 4%, and 0%, respectively, for invasion of the pericardium, the pulmonary vein, the phrenic nerve, the pulmonary artery, and the recurrent laryngeal nerve. The majority of the patients in this series, however, had concomitant N2 disease (68%), multiple sites of mediastinal involvement (48%), or invasion of major mediastinal structures (T4) (48%). As a result, only 22% of the 225 patients could have complete resection and 44% had totally unresectable disease. There was a 5-year survival advantage in patients treated with complete resection (9% versus 0%), in "incomplete" resection plus brachytherapy (22% versus 0%), and in patients with a clinically unsuspected T3 lesion (12% versus 5%).

Determination of technical resectability before operation as well as clinical distinction from bulky N2 disease is not always possible in these central T3 lesions, even with the help of modern medical imaging techniques. Induction therapy with the hope of increasing resectability and improving long-term survival should be further investigated in this group of patients with very poor prognostic lesions.

PROXIMAL AIRWAY INVOLVEMENT. A tumor in the main bronchus within 2 cm of the carina or with atelectasis of the entire lung (T3) can be treated by pneumonectomy or, if possible, sleeve lobectomy. The report of the group from Toronto General Hospital is one of the very few that looked specifically at the results after pneumonectomy for a lesion in the main bronchus [43]. In contrast, there is a surfeit of reports in the recent literature analyzing 5-year survival rates after sleeve lobectomy, although only few patients with a true T3 lesion were included [43–57].

The overall 5-year survival with both types of operations was in the range of 30% (Table 4). A 50% 5-year survival can be expected in the absence of nodal disease. If mediastinal lymph nodes are involved, virtually no

Table 4. Results After Surgical Treatment for NSCLC With Proximal Airway Involvement (T3)

First Author [Reference]	No. of Cases Operated	Est. 5-Year Survival (%)	Mortality (%)
Van Den Bosch [44]	50	41	8
Ungar [45]	99	54[a]	7
Eschapasse [46]	31	42	7
Keszler [48]	76	22[a]	6
Maeda [50]	23	13[a]	5
Vogt-Moykopf [51]	97	12	15
Naruke [54]	62	39	1

[a] Crude survival.

patient will experience long-term survival [44, 46, 49–51]. Therefore, some authors advocate not to offer operation if mediastinal lymph node involvement is documented preoperatively [47, 48]. Patients with incomplete resection had a poor prognosis with either resectional technique [43]. Therefore, operative frozen section of the bronchial and vascular resection margins should be carried out whenever resection is considered for a bronchogenic carcinoma invading the proximal airway and re-resection, if possible, should be performed in the presence of "positive" margins.

Operative mortality for sleeve lobectomy was reported in the range of 1% to 15% (see Table 4) compared with 6% for pneumonectomy [58]. Positive hilar lymph nodes, combined sleeve resection of the pulmonary artery, and compromised pulmonary function have all been identified as poor prognostic indicators after sleeve lobectomy [43, 44, 52, 56, 57]. Therefore, many authors have emphasized not to offer sleeve lobectomy if complete lymph node excision, as a result of this technique, is not possible.

N2 Disease

Metastasis to ipsilateral mediastinal and subcarinal lymph nodes is defined as N2 disease [8]. Less than 5% of all the patients with clinically apparent N2 disease will ultimately survive 5 years [8]. Unfortunately, about 40% to 45% of the patients with NSCLC will present in this fashion [11, 12, 59]. Considerable controversy exists regarding surgical treatment for patients with mediastinal lymph node metastasis.

MINIMAL N2 DISEASE. Several centers have recently reviewed their surgical results in N2 disease and most have stressed the importance of resection in a selected group of patients [11, 12, 15, 59–77]. Five-year survival rates were reported in the range of 10% to 20% in all patients undergoing thoracotomy and 20% to 30% if operation resulted in a complete resection of all disease (Table 5). There were virtually no long-term survivors after incomplete resection, where gross or microscopic residual disease was left behind [62, 69].

In a recent review, Shields [78] summarized the subgroup of patients with mediastinal lymph node involvement that might benefit from operation including those patients discovered to have resectable N2 disease at the time of thoracotomy or those few patients with technically resectable N2 disease discovered at mediastinoscopy. He correctly pointed out that one should realize that this subset of patients suitable for complete resection comprises only 10% of all patients with NSCLC and 20% of patients with N2 disease. Thus the 5-year survivors in this group with "minimal" N2 disease represent only 3% to 6% of all patients with involved mediastinal lymph nodes.

Radiologic evidence of N2 disease, positive mediastinoscopic findings, adenocarcinoma on histologic examination, high T status, subcarinal nodes, multiple or "high" mediastinal nodal levels, and extranodal disease have all been identified as adverse factors influencing survival after surgical resection in patients with N2 disease, although statistical significance was not always present or reported.

Whenever N2 disease is present, complete mediastinal lymph node dissection is warranted although its value (versus sampling) in earlier stage (N0–N1) disease has been argued. In two retrospective analyses [65, 69], the authors have found a survival advantage after mediastinal lymph node dissection for N2 disease compared with patients without mediastinal lymph node dissection (15.9% versus 6.7% 5-year survival) [69].

The role of postoperative adjuvant therapy has been extensively studied during the last 20 years [79]. The North American LCSG study evaluating the effect of

Table 5. Results After Surgical Treatment for NSCLC With N2 Disease

First Author [Reference]	No. of Patients	5-Year Survival (%)	Mortality (%)
All N2			
Kirschner [60]	45	20	0
Sawamura [65]	107	?	25
Mastrorilli [67]	108	?	2
Naruke [69]	426	14	10
Deneffe [72]	42	9	NS
Levasseur [74]	254	18	6
Watanabe [11]	153	17	3
Walker [75]	70	32[a]	10
Completely resected N2			
Kirsch [61]	136	21	4
Martini [63]	151	30[a]	1
Naruke [69]	242	19	10
Mountain [13]	118	21[b]	NS
Levasseur [74]	191	23	6
Watanabe [11]	84	24	3
Frytak [68]	101	19 (4 y)	NS
Mediastinoscopy +ve N2			
Pearson [62]	79	9	NS
Coughlin [64]	28	18	NS

[a] Adjusted for noncancer deaths. [b] Excluding operative deaths.

NS = not stated; +ve = positive.

postoperative radiotherapy in patients who underwent complete resection of a stage II or III squamous cell carcinoma could not demonstrate a significant survival advantage compared with patients not offered postoperative radiotherapy [80]. These latter findings confirmed the conclusions of two earlier prospective, randomized trials [81, 82]. Four other retrospective analyses, however, had previously concluded that patients with involved mediastinal lymph nodes can benefit from and therefore should receive postoperative irradiation [61, 83–85].

All these postoperative adjuvant radiation studies showed a striking reduction in local recurrence, but still a high systemic relapse rate, indicating that effective systemic therapy is mandatory before improved survival will be seen in this stage of disease.

The first LCSG study evaluating the role of postoperative chemotherapy (cyclophosphamide, doxorubicin, and cisplatin [CAP]) versus immunotherapy (intrapleural Calmette-Guérin bacillus and levamisole) in patients with completely resected stage II and III adenocarcinoma or large cell carcinoma showed a significant prolongation of median disease-free interval and median survival in the chemotherapy arm [86]. These findings are in contrast with results from studies in the early 1970s that failed to show a beneficial effect of adjuvant chemotherapy using a variety of less effective and often single-drug regimens [79]. The LCSG also investigated the role of postoperative radiotherapy alone versus postoperative combined radiotherapy plus chemotherapy (CAP) in patients with "incompletely resected," locally advanced NSCLC and showed a significant difference in median survival time (20 months versus 13 months) and in median time to recurrence (14 months versus 8 months), favoring the chemoradiotherapy arm [87]. Two further studies in which patients with T1 N1 or T2 N0 disease [88] or patients in stage II or III (LCSG, personal communication) were randomized to receive CAP chemotherapy or no further treatment after tumor resection did not demonstrate any advantage for the adjuvant chemotherapy. As yet, there is no definite evidence that adjuvant chemotherapy offers any survival benefit. The beneficial effect of chemoradiotherapy needs further confirmation and is the subject of a National Cancer Institute intergroup study.

BULKY N2 DISEASE. Extensive mediastinal lymphadenopathy evident from roentgenographic, bronchoscopic, or mediastinoscopic findings is considered by most surgeons to be unresectable, and radiotherapy has been used as definitive treatment. Surgeons have therefore always been interested in the benefit that induction (neoadjuvant) therapy before operation may offer patients with this more advanced type of N2 disease as well as with other unresectable stage IIIa+b lesions. The goals of preoperative, induction therapy are to reduce the tumor size in order to improve resectability and to decrease local recurrence as well as to treat potential micrometastatic disease several months before standard postoperative treatment.

Induction Treatment Plus Operation

Historical trials comparing preoperative radiotherapy in the range of 4,000 to 6,000 cGy with operation alone failed to show any survival benefit, but did show an increased resectability rate [89, 90]. However, these studies included patients with all stages of lung carcinoma. Nevertheless, preoperative radiation is still believed to be of value in locally invading lesions (T3 or T4) [91], especially superior sulcus tumors [27, 36]. The role of preoperative radiotherapy in locally advanced disease alone has not yet been investigated in a controlled fashion.

Recently, a surfeit of phase II studies have assessed the benefit of induction chemotherapy or chemoradiotherapy in patients with unresectable disease. Between 1984 and May 1991, 25 different studies have reported their preliminary or definitive results [92–116]. Fifteen trials used a combination of chemotherapy plus radiotherapy before operation and ten used induction chemotherapy alone. In all reports, chemotherapy consisted of a cisplatin-based, multidrug regimen. Different entry criteria as well as different drug regimens were used in these studies, making comparison very difficult. In total, induction therapy was administered to more than 1,000 patients. Clinical major response rates ranged between 38% and 86% with a mean of 62.1%. Fifty-five percent ultimately went to operation with an overall resection rate of 49.1% and a complete resection rate of 41.8%. Sterilization rates (pathologic complete responses over all patients entered in study) varied between 0% and 21% (mean of 11.7% overall, 9.7% for chemotherapy and 12.7% for chemotherapy plus radiotherapy). Median survival time ranged between 8 and 32 months with an average of 16.5 months. Drug-related morbidity and mortality as well as significant difficulties with surgical dissection were well recognized. However, operative mortality remained acceptable (Tables 6–8). Three- and 5-year survival in patients with initially "unresectable" N2 disease treated with induction therapy followed by operation have yet to be reported, but early reports suggest a 15% to 30% 5-year survival rate [95, 108].

These reports, compared with historical data, suggest that induction chemo/radiotherapy will increase the complete resection rate and may improve the overall survival in these patients with bulky N2 (see Tables 6–8) or other "unresectable" disease. Recently, preliminary findings of a randomized trial from M.D. Anderson Cancer Center comparing a small number of patients treated with chemotherapy (cyclophosphamide, etoposide, and cisplatin) followed by operation versus operation alone in stage IIIa NSCLC seem to confirm this hypothesis. Resectability rate was increased from 61% to 78% and 1-year survival improved from 34% to 76% after combined treatment [116].

In all studies using induction therapy before operation, whether radiotherapy alone, chemotherapy alone, or chemo/radiotherapy, local recurrence appears diminished, but systemic spread, especially to the brain, remains a major problem. Therefore, it is likely that intensive systemic therapy with effective agents will be a

Table 6. Results of Induction Chemotherapy Plus Operation for "Unresectable" IIIa Patients

First author [Reference]	Induction Regimen	RR (%)	No. of Cases		CR	Overall Survival			Operative Mortality (%)
			Total	Operated		MST (mo)	1-Year (%)	3-Year (%)	
Sridhar (109)	FEP[a]	62	21	19	10	12	. . .	. . .	NS
Burkes (111)	MVP	69	39	21	17	19	. . .	. . .	10%
Pisters (113)	MVP	77	73	58	44	19	72	26	1%
Lad (115)	MVP or RT	47	64	24	21	12	. . .	. . .	17%
Fossella (116)	CEP	67	12	8	4	. . .	76	. . .	NS

[a] Includes stage IV as well.

A = Adriamycin (doxorubicin); C = Cytoxan (cyclophosphamide); CR = completely resected; E = etoposide (VP-16); F = 5-fluorouracil; M = mitomycin-C; MST = median survival time; NS = not stated; V = vindesine or vinblastine; P = Platinol (cisplatin); RT = radiotherapy; RR = response rate.

necessary part of treatment before survival is improved. The use of these induction therapy programs is still reserved for carefully designed clinical trials.

Radiotherapy

Radiation therapy with standard fractionation (6,000 cGy to the primary tumor and mediastinum in 30 fractions over 6 weeks) with curative intent is still accepted as standard treatment in those patients suffering from locally advanced unresectable IIIa disease. Although this form of treatment has an objective impact on local tumor control with response rate ranging between 40% and 60% [117], median survival is still expected to be less than 10 months and only 3% to 5% of patients will experience long-term survival owing to systemic recurrence. A recent trial completed by the Radiation Therapy Oncology Group demonstrated that hyperfractionated radiation therapy with a total dose of 69.6 Gy showed significantly better results in these patients, with a median survival of 13 months and a 2-year survival of 29% [118].

Over the last 10 years, several comparative randomized trials have evaluated the value of induction chemotherapy followed by radiation for unresectable stage III disease [119]. Recently, two of these trials have demonstrated a doubled 2-year survival (32% versus 14%) [120] and 3-year survival (23% versus 11%) [121] in patients treated in this way compared with radiation therapy alone. The overall response rate reached 60%, and median survival approximated 14 to 15 months [120, 121]. Survival results using radiotherapy as the principle treatment for clinical N2 disease in recently reported studies are listed in Table 9. These results compare favorably with those using a surgical approach.

Randomized phase III clinical trials comparing induction chemotherapy or chemo/radiotherapy plus operation with nonsurgical treatment (radiotherapy or chemo/radiotherapy) are underway to finally answer these questions. Definitive conclusions as to whether induction therapy plus operation can offer better and longer survival than standard radiotherapeutic approaches in this group of patients must await the results of these trials.

Stage IIIb

Stage IIIb is defined to comprise patients with an "unresectable" T4 or N3 lesion [8]. Radiation therapy, chemotherapy, or a combination of both remains the standard treatment for these patients [123]. In general, they are not

Table 7. Results of Induction Chemoradiotherapy Plus Operation for "Unresectable" IIIa, b(IV) Patients Where Median Survival Times or 1-Year Survival Were Reported

First author [Reference]	Induction Regimen	RR (%)	No. of Cases		Resection	Overall Survival			Operated Mortality
			Total	Operated		MST (mo)	1-Year (%)	3-Year (%)	
Eagan [93]	CAP + RT	51	39	20	19	11	43	. . .	0
Skarin [95]	CAP + RT	72	41	37	36	32	75	31	5%
Elias [96]	CAP ± RT	43	39	. . .	21	31	. . .	45	NS
Faber [98]	F ± EP + RT	38	85	62	60	22	. . .	40	5%
Henriquez [99]	MVP + RT[a]	68	53	33	. . .	15	. . .	. . .	NS
Weitberg [100]	EP + RT	86	44	27	21	16	60	. . .	NS
Rebischung [104]	FVP + RT[a]	77	30	. . .	16	14	. . .	. . .	NS
Bedini [105]	P + RT[a]	86	50	. . .	23	. . .	64	. . .	4%
Weiden [106]	FP + RT[a]	56	85	54	45	13	. . .	. . .	7%

[a] Stage IIIa and IIIb disease.

A = Adriamycin (doxorubicin); C = Cytoxan (cyclophosphamide); E = etoposide (VP-16); F = 5-fluorouracil; M = mitomycin-C; MST = median survival time; NS = not stated; V = vindesine or vinblastine; P = Platinol (cisplatin); RR = response rate.

Table 8. Results of 25 Studies of Induction Therapy Plus Operation in Stage IIIa and IIIb Disease[a]

Induction Regimen	No. of Studies	No. of Cases	Response Rate	Sterilization Rate	Complete Resectability	MST (mo)	Operative Mortality
CT	10	393	66%	10%	44%	13.5	9%
CT-RT	15	695	60%	13%	39%	18.8	6.6%
Total	25	1,088	62%	12%	42%	16.5	7.5%

[a] References [92–116].

CT = chemotherapy; MST = median survival time; RT = radiotherapy.

referred for surgical treatment. Nevertheless, in a large retrospective study, resected patients postoperatively classified as stage IIIb still had an overall 5-year survival of 6% [14] and therefore can occasionally be totally cured of their disease.

T4 Tumors

Tumors invading mediastinal structures such as the carina and trachea, the heart and great vessels, the esophagus, or vertebral body, as well as tumors associated with the presence of a malignant pleural effusion, are all classified as T4 lesions [8]. In the series of Naruke and co-authors [14], 5-year survival in 104 patients after resection of such a T4 lesion was 8%.

CARINAL INVASION. Primary lung cancer invading the carina, whether by (sub)mucosal spread or extrabronchial tumor, is considered unresectable by most thoracic surgeons. However, pneumonectomy with tracheal sleeve resection and direct reanastomosis of the trachea to the contralateral main bronchus is advocated by some surgeons with reported 5-year survival approaching 20% [53, 124–130] (Table 10). Mediastinal nodal involvement makes the prognosis much worse, such that most surgeons do not advocate resection if N2 disease is found preoperatively [125, 126, 128, 130].

Anastomotic dehiscence with bronchial fistula formation and adult respiratory distress syndrome [130] are major postoperative problems and are the main cause of the high operative mortality, varying from 11% to 27% in large series (see Table 10). As the operative mortality rate may exceed the long-term survival rate, sleeve pneumonectomy should be reserved for a very select group of patients. Careful preoperative assessment including extensive cardiopulmonary function testing and mediastinoscopy to rule out the possibility of N2 disease is recommended.

The use of perioperative irradiation may be of benefit to prevent the serious problem of local recurrence [53, 130]. However, preoperative radiation therapy can compromise tracheal healing and may contribute to the lethal complication of anastomotic dehiscence and adult respiratory distress syndrome.

INVASION OF SUPERIOR VENA CAVA. Involvement of the superior vena cava has been treated occasionally by resection and graft replacement [131–133]. Long-term survivors reported in the literature are limited to case reports [133]. In the series from Memorial Sloan-Kettering Cancer Center, there were no 5-year survivors after resection in 18 patients with superior vena caval invasion [40]. Preoperative distinction of superior vena caval invasion by the tumor itself (T4) or its involved lymph nodes (N2) is not always possible. As with T3 lesions, N2 disease will worsen the prognosis significantly such that preoperative mediastinoscopy to exclude mediastinal lymph node involvement is justified if superior vena caval invasion by the primary tumor is to be treated surgically. Reported series include only few cases, so that the significance of this finding cannot be assessed with regard to curability.

Table 9. Survival Results Using Radiotherapy as the Principal Treatment for Clinical N2 Disease in Recently Reported Prospective Studies

Investigators [Reference]	Treatment	No. of Patients	MST (mo)	Survival (%) 1 Year	Survival (%) 3 Years
RTOG [122]	SFX-RT (60 Gy)	59	8[a]	30	7
RTOG [122]	HFX-RT (69.6 Gy)	50	14[a]	58	20
CALGB [121]	VP + RT	78	14	55	23

[a] Extracted from survival curve.

CALGB = Cancer and Leukemia Group B; HFX-RT = hyperfractionated radiation therapy; MST = median survival time; RTOG = Radiation Therapy Oncology Group; SFX-RT = standard fractionation radiation therapy; VP + RT = vindesine and cisplatin + radiotherapy.

Table 10. Reported Results After Surgical Treatment for NSCLC With Carinal Invasion (T4)

First Author [Reference]	No. of Cases Operated	Est. 5-Year Survival (%)	Mortality (%)
Deslauriers [124]	26	23[a]	27
Fujimura [125]	15	0	NS
Faber [53]	33	15[a]	24
Dartevelle [126]	55	23	11
Mastrorilli [127]	11	20	0
Tsuchiya [128]	20	59 (2 y)	15
Vogt-Moykopf [129]	59	30 (2 y)	14
Mathisen [130]	37	19	19

[a] Crude survival.

NS = not stated.

INVASION OF MYOCARDIUM, AORTA, ESOPHAGUS, AND VERTEBRAL BODY. Surgical resection resulting in complete excision of a primary tumor with mediastinal organ invasion is often not possible. Palliative incomplete resections have not demonstrated survival benefit. In the series from Memorial Sloan-Kettering Cancer Center, although not all patients underwent resection of the primary tumor or part of the invaded organ, there were no 5-year survivors in 19 patients with involvement of aorta or in 3 patients with invasion of the atrium, but 1 patient of 7 (14%) with invasion of the esophagus lived beyond 5 years [40]. Despite these disappointing results, limited invasion of the atrial wall can sometimes result in a complete resection with the hope of an occasional cure, and en bloc resection of the lung with part of the involved aorta [132], esophagus, or vertebral body, not uncommon in superior sulcus tumors [134], may result in long-term survival for the very occasional patient. Postoperative radiotherapy may be of benefit in these cases to improve local control.

MALIGNANT PLEURAL EFFUSION. According to the new TNM staging system, a preoperatively diagnosed bloody or exudative pleural effusion should be considered malignant (cT4), regardless of the presence or absence of malignant cells in the fluid [8]. Approximately 5% to 10% of the patients with lung cancer will have a serious pleural effusion, not always malignant, as a result of atelectasis, obstructive pneumonitis, lymphatic or venous obstruction, or a pulmonary embolus.

The finding of a serious pleural effusion is a poor prognostic sign [16]. Mean survival in these patients is only 3 to 6 months with a negligible 5-year survival [41, 135, 136]. For this reason, physicians believe that these patients are biologically inoperable and therefore should not be treated surgically. A review from the Mayo Clinic demonstrated that even cytologically negative pleural effusions were predictive of surgical unresectability in 95% of these patients [137]. Nevertheless, 5% of them were found on thoracotomy to have limited, resectable disease and all were long-term survivors. The authors of this review concluded that, in patients with cytologically negative pleural effusions, unresectability must be documented surgically. On the other hand, Naruke and coworkers [14] reported 11% 5-year survival in 48 patients with a documented malignant pleural effusion compared with 40% in 112 patients with a nonmalignant effusion, identical to the 5-year survival in 1,298 patients without effusion. The treatment modality in these patients with a positive effusion was not specified. Recently, 6 patients with a malignant pleural effusion from NSCLC without further spread outside the hemithorax were treated at Roswell Park Cancer Institute with pleuropneumonectomy preceded by a cisplatinum-based chemotherapeutic drug regimen, resulting in a median survival of 24 months [138].

Thoracentesis with cytologic examination of the pleural fluid has a high false-negative rate approaching 65% [139]. Thoracoscopy with pleural biopsy is an excellent diagnostic tool, yielding a diagnosis in more than 90% of the patients and avoiding an unnecessary thoracotomy [139–141]. Every attempt should be made to rule out malignancy as the cause of the pleural effusion.

N3 Disease

The presence of an involved contralateral hilar, contralateral mediastinal, or any scalene or supraclavicular lymph node is defined as N3 disease [8]. Identified preoperatively, these patients are generally denied surgical treatment because standard excision of the primary tumor and its involved lymph nodes will not result in a complete resection.

So far, in large series, there have been no 5-year survivors after surgical treatment for N3 disease [14, 135]. Recently, a few reports from Japan have advocated the use of a median sternotomy for radical mediastinal and cervical lymph node dissection after standard resection of lung cancer with involved mediastinal nodes [142–144]. Hata and co-workers [143] reported a 60% 2-year survival in 9 patients with N3 disease using this technique. We await long-term follow-up.

The Southwest Oncology Group recently reported their interim findings in a study (SWOG 8805) using concurrent chemotherapy (cisplatin and VP-16) and chest irradiation followed by operation for stage IIIa and IIIb disease [101]. Seventy-four percent of the patients with a clinical response or stable disease finally went to operation. Although the number of N3 patients was not specified, 15 of 19 patients (79%) with a stage IIIb lesion undergoing thoracotomy had a complete resection. Further investigation of the role of induction chemoradiotherapy in such patients in properly designed clinical trials is indicated. On the whole, however, N3 disease should still be considered a definitive sign of inoperability.

Stage IV

Stage IV comprises all patients with distant metastases (M1) [8]. When first seen, more than 50% of all NSCLC patients have extrathoracic metastases, often at multiple locations [145]. The median survival in patients with metastatic carcinoma of the lung is measured in months to weeks, and only a few will survive beyond 1 year. Conventional teaching therefore suggests that extrathoracic spread implies biological inoperability and incurability. Initial performance status, prior weight loss, and serum lactic dehydrogenase level are the most important prognostic factors predicting survival in these patients [146–148].

Non–small cell lung cancer can metastasize anywhere. In descending order, hematogenous spread to the bone, brain, contralateral lung, liver, adrenal gland, skin, and the ipsilateral lung are the most common sites when initially seen [145].

Multidrug platinum-based chemotherapy regimens in selected stage IV patients with good performance status were demonstrated over the last 10 years to palliate symptoms and improve median survival [149]. In a Canadian multicenter trial, combination chemotherapy alone using CAP or a combination of vindesine and cisplatin was shown to prolong median survival significantly in patients with advanced (stage III and IV) disease compared with supportive care alone (7.6 months for vindesine and cisplatin, 5.8 months for CAP, 4.0 months for supportive care) [150]. Local radiotherapy, whether external beam radiation or endobronchial brachytherapy [151], and neodymium:yttrium-aluminum garnet laser treatment [152] are now well-accepted and successful treatment modalities in the palliation of symptoms at the primary or metastatic site.

However, when the primary lung cancer is well controlled or is expected to be completely resectable and when extensive metastatic screening tests fail to demonstrate further extrathoracic disease, removal of a solitary metastatic lesion may improve survival and afford the best palliation.

In a large series reviewing the prognosis in 1,737 patients with a resected lung carcinoma, overall 5-year survival in 258 patients with an M1 lesion was 7.5% [14]. However, most of these M1 lesions were located in the ipsilateral lung (56.6%), and all long-term survivors were derived from this group. Recent reports also suggest that solitary brain metastasis should be approached aggressively.

M1 LUNG. Distinction between a second primary lung cancer and a metastasis in synchronous lung lesions or between local recurrence, a new primary lung cancer, and a pulmonary metastasis from a previous resected lung cancer in metachronous lung lesions is not always obvious [153–159]. Establishing appropriate criteria to distinguish a metastatic lesion from other recurrent cancer is critical as this can have significant clinical and therapeutic implications. A second or recurrent lung lesion may be considered a metastasis if the histology is similar to the primary tumor, occurring in the opposite lung or in an area of the lung not contiguous to the respected tumor or its ipsilateral regional lymphatic drainage. Its metastatic nature is very likely when further extrathoracic cancer spread is evident or when multiple nodules are present in the lung.

In a unique article from Deslauriers and co-authors [160], the presence of satellite nodules, clearly separated from the primary tumor but with identical histologic characteristics, was found to be a poor prognostic factor. In patients with satellite nodules from all stages of lung cancer, 5-year survival was 21.6% compared with 44% if no nodules were present. However, Deslauriers and co-authors believed that these satellite nodules should be considered as locally advanced disease (T3) rather than metastasis (M1). The mechanism of tumor spread in the lung is not well known, but theoretically satellite nodules may develop as a result of a blood-borne or an air-borne metastasis from a primary bronchogenic carcinoma. The new TNM staging system also fails to specifically classify these synchronous (whether a new primary tumor or a metastasis) lung lesions.

The same criteria in selecting patients for surgical resection of a pulmonary metastasis from a primary lung cancer should be maintained as in patients with metastatic carcinoma to the lung from other primary tumors [161]. If a solitary synchronous lesion is discovered in a different lobe from the primary tumor, resection of both lesions is the treatment of choice whenever possible.

Table 11. Reported Results After Combined Resection for Primary NSCLC With a Single Brain Metastasis (M1)

First Author [Reference]	Year	No. of Cases Combined Operation	5-Year Survival (%)	Combined Mortality (%)
Salerno [166]	1979	23	13	22
Winston [167]	1980	22	9 (2 y)	10
White [168]	1981	38	15 (2 y)	6
Mussi [171]	1985	20	34	0
Ehrenhaft [174]	1986	40	12	2
Magilligan [162]	1986	41	21	2
Read [178]	1989	27	21	0
Macchiarini [179]	1991	37	30	0
Burt [183]	1991	185	13	3

M1 BRAIN. Brain metastases constitute nearly one third of all observed recurrence in patients with resected NSCLC. Autopsy data suggest that the incidence may be greater than 50%, the majority in patients with adenocarcinoma [162]. In a review by the LCSG, the brain was the sole site of first recurrence in only 6.4% of patients with completely resected NSCLC [163] but accounted for approximately 20% of all recurrences. Nearly half of the patients seen with brain metastases have solitary lesions on computed tomographic scan [164]. With symptoms, median survival without therapy is limited to only 1 month. Corticosteroids and whole-brain irradiation can offer effective palliation of symptoms but will only modestly increase survival by 2 and 3 to 6 months, respectively [165].

Solitary brain metastasis is best treated, whenever possible, by surgical resection; 5-year survival is in the range of 10% to 20% [162, 166–183] (Table 11). Surgical excision of brain metastasis no matter the primary site (approximately 75% from NSCLC) followed by radiation was shown in a randomized study to be superior to radiotherapy alone in prolonging median survival (9.2 versus 3.4 months), in preventing local recurrence, and in providing a better quality of life [184].

Many factors have been identified as negative prognostic signs. The significant one appears to be the ability to completely resect the primary tumor and solitary metastatic focus, and in such cases a 15% to 30% 5-year survival is quoted. A recent analysis of 185 patients undergoing resection of a solitary brain metastasis from NSCLC at Memorial Sloan-Kettering Cancer Center demonstrated an overall 5- and 10-year survival of 13% and 7%, respectively [183]. Among 120 patients having had resection of a synchronous solitary brain metastasis, 5-year survival was significantly prolonged in the 32 patients who had complete resection of their primary lung tumor compared with 88 patients who had incomplete or no resection (16% versus 4%, respectively). This was independent of the locoregional (TN) stage of the NSCLC. The authors of that analysis concluded that locoregional extent of the NSCLC should not preclude resection of both the primary disease and the brain metastasis, as long as both are completely resectable.

Martini [165] described the current view regarding surgical management of synchronous and metachronous solitary brain metastases from NSCL. In metachronous lesions, resection of the brain metastasis should be considered if no other site of recurrence is demonstrated. In synchronous lesions, if both lesions are detected simultaneously, craniotomy is done first and thoracotomy shortly thereafter whether or not the patient has neurologic symptoms. If either the lung or brain lesion is suspected to be unresectable, surgical treatment is directed first to the site where resectability is questioned most. Otherwise radiation therapy should be advocated.

M1 ADRENAL. Autopsy data report adrenal metastases from bronchogenic carcinoma to be found in about one third of the patients. Routine upper abdominal scanning techniques in the preoperative staging of NSCLC may reveal an adrenal mass in about 10% of the patients [185, 186]. Despite this, computed tomographic scan was reported to have a low sensitivity for the detection of adrenal metastatic lesions, especially in normal-sized glands [187]. To distinguish a suspicious lesion from a benign adenoma, present in about 2% of the population, cytologic confirmation of malignancy should be obtained using a computed tomography-guided fine-needle aspiration.

There have been isolated case reports of adrenalectomy for solitary adrenal metastasis from NSCLC [188–190], and long-term survival after combined excision of the primary tumor and its metastatic lesion has occurred [188]. The ultimate role of such an aggressive approach has yet to be defined.

M1 LIVER, BONE, AND SKIN. There have been no reports of long-term survival after combined surgical excision of a primary lung cancer with a solitary liver, bone, or skin mestastasis. It is rare that these lesions are truly solitary metastatic foci.

Conclusion

In patients with NSCLC, operation resulting in complete removal of the primary tumor, its involved lymph nodes, and even its solitary metastatic lesions remains the most effective mode of treatment. Therefore, this treatment modality should be made available whenever possible.

Survival results after resectional operation are closely related to the stage of disease (see Table 1). In stage IIIa, approximately 30% of the patients with T3 tumors invading the chest wall, the superior sulcus, the diaphragm, the mediastinal pleura, or pericardium will experience prolonged survival, and up to 50% when mediastinal lymph nodes are free of tumor. In the presence of N2 disease, only a very selected group with minimal mediastinal lymph node involvement (10% of all NSCLC patients and 20% of all N2 patients) are considered as primary surgical candidates with an estimated 5-year-survival ranging between 15% and 20% overall and up to 30% if complete resection can be achieved. However, these long-term survivors comprise only 3% to 6% of all N2 patients.

Operation preceded by induction chemo/radiotherapy is still an experimental approach for patients with bulky N2 disease. Until the results of ongoing comparative randomized trials have become available, radiotherapy remains the standard treatment for these patients.

The combination of a T3 lesion and involved mediastinal lymph nodes carries a very dismal prognosis because virtually no patient will experience prolonged survival. Therefore it is questionable whether these patients should have primary resection if mediastinal node invasion is demonstrated on preoperative mediastinoscopy.

In stage IIIb, where the primary tumor invades the carina (T4), selected patients may benefit from pneumonectomy in combination with carinal resection with an expected 5-year survival of approximately 20%. Patients with lung cancer invading other mediastinal organs (T4) will only occasionally live beyond 5 years after a major operation. It is important to realize that resectional operation in these stages of disease also carries a higher morbidity and mortality rate [58, 191]. Selectivity is therefore very important whenever surgical resection is being offered to these patients. In the presence of a malignant pleural effusion (T4) or involvement of supraclavicular or contralateral mediastinal lymph nodes (N3), operation has not demonstrated any advantage.

In stage IV disease, combined resection of the primary tumor and a single metastatic lesion, especially to the brain, may provide long-term survival in patients proved not to have other systemic disease.

Operation, however, does not always result in complete resection of the primary tumor and its locoregional lymph nodes and is certainly not an effective treatment for microscopic disseminated disease. Postoperative adjuvant radiotherapy can be effective in obtaining local control. Adjuvant chemotherapy can prolong median survival in advanced disease. However, as yet, no long-term survival benefit has been demonstrated from either treatment modality used in an adjuvant setting.

Several phase II trials using preoperative induction chemo/radiotherapy for initially "unresectable" disease have already published provocative data. However, randomized trials still have to prove the benefit of these combined modality treatments over operation alone in increasing resectability rate and over chemo/radiotherapy alone in prolonging survival. The continuing high incidence of deaths due to distant metastases underscores the need to combine more effective systemic therapy with surgical treatment if we are to expect a major impact on survival.

References

1. Boring CC, Squires TS, Tong T. Cancer statistics, 1991. CA 1991;41:19–36.
2. Carter D, Eggleston JC. Tumors of the lower respiratory tract. In: Atlas of tumor pathology, second series, fascicle 17. Washington, DC: Armed Forces Institute of Pathology, 1983.
3. Humphrey EW, Smart CR, Winchester DP, et al. National

survey of the pattern of care for carcinoma of the lung. J Thorac Cardiovasc Surg 1990;100:837–43.

4. Martini N. Surgical treatment of non–small cell lung cancer by stage. Semin Surg Oncol 1990;6:248–54.
5. Talton BM, Constable WC, Kersh R. Curative radiotherapy in non–small cell carcinoma of the lung. Int J Radiat Oncol Biol Phys 1990;19:15–21.
6. Haffty BG, Goldberg NB, Gerstley J, et al. Results of radical radiation therapy in clinical stage I technically operable non–small cell lung cancer. Int J Radiat Oncol Biol Phys 1988;15:69–73.
7. Noordijk EM, v d Poest Clement E, Hermans J, Wever AMJ, Leer JWH. Radiotherapy as an alternative to surgery in elderly patients with resectable lung cancer. Radiother Oncol 1988;13:83–9.
8. Mountain CF. A new international staging system for lung cancer. Chest 1986;89:225S–33S.
9. American Joint Committee for Cancer Staging and End Results Reporting. Clinical staging system for carcinoma of the lung. Chicago: American Cancer Society, 1973.
10. Renault P, Merlier M, Lange J. La codification TNM applique aux cancers broncho-pulmonaires operes. Rev Fr Mal Resp 1975;3:59–64.
11. Watanabe Y, Shimizu J, Oda M, et al. Aggressive surgical intervention in N2 non–small cell cancer of the lung. Ann Thorac Surg 1991;51:253–61.
12. Martini N, Flehinger BJ, Zaman MB, Beattie JB. Prospective study of 445 lung carcinomas with mediastinal lymph node metastases. J Thorac Cardiovasc Surg 1980;80:390–9.
13. Mountain CF. The biological operability of stage III non–small cell lung cancer. Ann Thorac Surg 1985;40:60–4.
14. Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. J Thorac Cardiovasc Surg 1988;96:440–7.
15. Mountain CF. Expanded possibilities for surgical treatment of lung cancer. Survival in stage IIIa disease. Chest 1990;97: 1045–51.
16. Mountain CF. Prognostic implications of the international staging system for lung cancer. Semin Oncol 1988;15: 236–45.
17. Cromartie RS, Parker EF, May JE, et al. Carcinoma of the lung: a clinical review. Ann Thorac Surg 1980;30:30–5.
18. Paone JF, Spees EK, Newton CG, et al. An appraisal of en bloc resection of peripheral bronchogenic carcinoma involving the thoracic wall. Chest 1982;81:203–7.
19. Patterson GA, Ilves R, Ginsberg RJ, et al. The value of adjuvant radiotherapy in pulmonary and chest wall resection for bronchogenic carcinoma. Ann Thorac Surg 1982;34: 692–7.
20. Piehler JM, Pairolero PC, Weiland LH, et al. Bronchogenic carcinoma with chest wall invasion: factors affecting survival following en bloc resection. Ann Thorac Surg 1982;34: 684–91.
21. McCaughan BC, Martini N, Bains MS, McCormack PM. Chest wall invasion in carcinoma of the lung. Therapeutic and prognostic implications. J Thorac Cardiovasc Surg 1985; 89:836–41.
22. Van de Wal HJ, Lacquet LK, Jongerius CM. Chirurgische behandeling van longtumoren met doorgroei in de thoraxwand. Tijdschr Geneeskd 1987;43:91–6.
23. Carrel T, Nachbur B, Bleher A. Is radiotherapy prior to surgical resection indicated for bronchogenic carcinoma with chest wall infiltration and for Pancoast tumors [Abstract]? Lung Cancer 1988;4:A80.
24. Ratto GB, Piacenza G, Frola C, et al. Chest wall involvement by lung cancer: computed tomographic detection and results at operation. Ann Thorac Surg 1991;51:182–8.
25. Allen MS, Mathisen DJ, Grillo HC, et al. Bronchogenic carcinoma with chest wall invasion. Ann Thorac Surg 1991; 51:948–51.
26. Stanford W, Barnes RP, Tucker AR. Influence of staging in superior sulcus (Pancoast) tumors of the lung. Ann Thorac Surg 1980;29:406–9.
27. Paulson DL. The "superior sulcus" lesion. In: Delarue NC, Eschapasse H, eds. International trends in general thoracic surgery, vol 1: lung cancer. Philadelphia: Saunders, 1985: 121–31.
28. Anderson TM, Moy PM, Homes EC. Factors affecting survival in superior sulcus tumors. J Clin Oncol 1986;4:1598–603.
29. Devine JW, Mendenhall WM, Million RR, Carmichael MJ. Carcinoma of the superior sulcus treated with surgery and/or radiation therapy. Cancer 1986;57:941–3.
30. Beyer DC, Weisenburger T. Superior sulcus tumors. Am J Clin Oncol 1986;9:156–61.
31. Rice TW, Pringle JF, Sinclair JE, et al. Superior sulcus tumors: results of treatment [Abstract]. Lung Cancer 1986; 2:156–7.
32. Shahian DM, Neptune WB, Ellis FH. Pancoast tumors: improved survival with preoperative and postoperative radiotherapy. Ann Thorac Surg 1987;43:32–8.
33. Wright CD, Moncure AC, Shepard JAO, et al. Superior sulcus tumors: results of combined treatment (irradiation and radical resection). J Thorac Cardiovasc Surg 1987;94: 69–74.
34. Miller JI. Discussion of: Shahian DM, Neptune WB, Ellis FH. Pancoast tumors: improved survival with preoperative and postoperative radiotherapy. Ann Thorac Surg 1987;43: 32–8.
35. McKneally M. Discussion of: Shahian DM, Neptune WB, Ellis FH. Pancoast tumors: improved survival with preoperative and postoperative radiotherapy. Ann Thorac Surg 1987;43:32–8.
36. Hilaris BS, Martini N, Wong GY, Nori D. Treatment of superior sulcus tumor (Pancoast tumor). Surg Clin North Am 1987;67:965–77.
37. Ricci C, Rendina EA, Venuta F. Surgical treatment of superior sulcus tumors [Abstract]. Lung Cancer 1988;4(Suppl): A95.
38. Dartevelle P, Marzelle J, Chapelier A, Loc'h F. Extended operations for T3–T4 primary lung cancers; indications and results. Chest 1989;96:51S–3S.
39. Komaki R, Mountain CF, Holbert JM, et al. Superior sulcus tumors: treatment selection and results for 85 patients without metastasis (M0) at presentation. Int J Radiat Oncol Biol Phys 1990;19:31–6.
40. Burt ME. Pomerantz AH, Bains MS. Results of surgical treatment of stage III lung cancer invading the mediastinum. Surg Clin North Am 1987;67:987–1000.
41. Nakahashi H, Yasumoto K, Ishida T, et al. Results of surgical treatment of patients with T3 non–small cell lung cancer. Ann Thorac Surg 1988;46:178–81.
42. Trastek VF, Pairolero PC, Piehler JM, et al. En bloc (non–chest wall) resection for bronchogenic carcinoma with parietal fixation. J Thorac Cardiovasc Surg 1984;87:352–8.
43. Weisel RD, Cooper JD, Delarue NC, Theman TE, Todd RJ. Sleeve lobectomy for carcinoma of the lung. J Thorac Cardiovasc Surg 1979;78:839–49.
44. Van Den Bosch JMM, Bergstein PGM, Laros CD, Gelissen HJ, Schaepkens van Riempst ALEMS, Wagenaar SS. Lobectomy with sleeve resection in the treatment of tumors of the bronchus. Chest 1991;80:154–7.
45. Ungar I, Gyeney I, Scherer E, Szarvas I. Sleeve lobectomy: an alternative to pneumonectomy in the treatment of bronchial carcinoma. Thorac Cardiovasc Surg 1981;29:41–6.
46. Eschapasse H. Proceedings of the minisymposia of the IV world conference on lung cancer. Toronto, 1985:52–3.
47. Deslauriers J, Gaulin P, Beaulieu M, et al. Long term clinical and functional results of sleeve lobectomy for primary lung cancer. J Thorac Cardiovasc Surg 1986;92:871–9.
48. Keszler P. Sleeve resection and other bronchoplasties in the surgery of bronchogenic tumors. Int Surg 1986;71:229–32.
49. Sartori F, Binda R, Spreafico G, et al. Sleeve lobectomy in

the treatment of bronchogenic carcinoma. Int Surg 1986;71: 233–6.
50. Maeda M, Nanjo S, Nakamura K, Nakamoto K. Tracheobronchoplasty for lung cancer. Int Surg 1986;71:221–8.
51. Vogt-Moykopf I, Fritz T, Meyer G, et al. Bronchoplastic and angioplastic operation in bronchial carcinoma: long term results of a retrospective analysis from 73–83. Int Surg 1986;71:211–20.
52. Frist WH, Mathisen DJ, Hilgenberg AD, Grillo HC. Bronchial sleeve resection with and without pulmonary resection. J Thorac Cardiovasc Surg 1987;93:350–7.
53. Faber LP. Results of surgical treatment of stage III lung carcinoma with carinal proximity. The role of sleeve lobectomy versus pneumonectomy and the role of sleeve pneumonectomy. Surg Clin North Am 1987;67:1001–14.
54. Naruke T. Bronchoplastic and bronchovascular procedures of the tracheobronchial tree in the management of primary lung cancer. Chest 1989;96:53S–6S.
55. Van Schil PE, Brutel de la Rivière A, Knaepen PJ, van Swieten HA, Defauw JJ, van den Bosch JM. TNM staging and long-term follow-up after sleeve resection for bronchogenic tumors. Ann Thorac Surg 1991;52:1096–101.
56. Firmin RK, Azariades M, Lennox SC, et al. Sleeve lobectomy (lobectomy and bronchoplasty) for bronchial carcinoma. Ann Thorac Surg 1983;35:442–9.
57. Belli L, Meroni A, Rondinara G, Beati C. Bronchoplastic procedures and pulmonary artery reconstruction in the treatment of bronchogenic cancer. J Thorac Cardiovasc Surg 1985;90:167–71.
58. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty-day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 1983;86:654–8.
59. Martini N, Flehinger BJ, Zaman MB, Beattie JB. Results of resection in non–oat cell carcinoma of the lung with mediastinal lymph node metastasis. Ann Surg 1983;198:386–97.
60. Kirschner PA. Lung cancer: preoperative radiation therapy and surgery. N Y State J Med 1981;81:339–42.
61. Kirsch MM, Sloan H. Mediastinal metastasis in bronchogenic carcinoma: influence of postoperative irradiation, cell type and location. Ann Thorac Surg 1982;33:459–63.
62. Pearson FG, Delarue NC, Ilves R, et al. Significance of positive superior mediastinal nodes identified at mediastinoscopy in patients with resectable cancer of the lung. J Thorac Cardiovasc Surg 1982;83:1–11.
63. Martini N, Flehinger BJ. The role of surgery in N2 lung cancer. Surg Clin North Am 1987;67:1037–49.
64. Coughlin M, Deslauriers J, Beaulieu M, et al. Role of mediastinoscopy in pretreatment staging of patients with primary lung cancer. Ann Thorac Surg 1985;40:556–60.
65. Sawamura K, Mori T, Hashimoto S, et al. Results of surgical treatment for N2 disease [Abstract]. Lung Cancer 1986;2:96.
66. Patterson GA, Piazza D, Pearson FG, et al. Significance of metastatic disease in subaortic lymph nodes. Ann Thorac Surg 1987;43:155–9.
67. Mastrorilli M, Bragaglia RB, Cipolla G, et al. Surgical management of N2 lung cancer [Abstract]. Lung Cancer 1988; 4(Suppl):A97.
68. Frytak S, Eagan RT, Sawamura K, et al. Treatment of "limited" stage III non–small cell carcinoma of the lung. Cancer Invest 1988;6:193–207.
69. Naruke T, Goya T, Tsuchiya R, Suemasu K. The importance of surgery to non–small cell carcinoma of lung with mediastinal lymph node metastasis. Ann Thorac Surg 1988;46: 603–10.
70. Naruke T, Suemasu K, Ishikawa S. Lymph node mapping and curability at various levels of metastasis in resected lung cancer. J Thorac Cardiovasc Surg 1978;76:832–9.
71. Hirono T, Koike T, Takizawa T, Eguchi S. Surgical treatment of N2 non–small cell lung cancer [Abstract]. Lung Cancer 1988;4(Suppl):A90.
72. Deneffe G, Stalpaert G. Five year survival in resected T3/N2 lung cancer. Acta Chir Belg 1989;89:159–60.
73. Ishida T, Yano T, Maeda K, et al. Strategy for lymphadenectomy in lung cancer three centimeters or less in diameter. Ann Thorac Surg 1990;50:708–13.
74. Levasseur PH, Regnard JF. Long-term results after surgery for N2 non–small cell lung cancer. Presented at the IASLC workshop, June 17–21, 1990, Bruges, Belgium.
75. Walker WS, Carey F, Cameron EWJ, Lamb D. Results of surgery for N2 status bronchial carcinoma. Presented at the IASLC workshop, June 17–21, 1990, Bruges, Belgium.
76. Thomas PA, Piantadosi S, Mountain CF, Lung Cancer Study Group. Should subcarinal lymph nodes be routinely examined in patients with non–small cell lung cancer? J Thorac Cardiovasc Surg 1988;95:883–7.
77. Ratto GB, Mereu C, Motta G. The prognostic significance of preoperative assessment of mediastinal lymph nodes in patients with lung cancer. Chest 1988;93:807–13.
78. Shields TW. The significance of ipsilateral mediastinal lymph node metastasis (N2 disease) in non–small cell carcinoma of the lung. J Thorac Cardiovasc Surg 1990;99:48–53.
79. Holmes EC. Surgical adjuvant therapy of non–small cell lung cancer. J Surg Oncol 1989;41(Suppl 1):26–33.
80. Weisenburger TH, Gail M for the Lung Cancer Study Group. Effects of postoperative mediastinal radiation on completely resected stage II and stage III epidermoid cancer of the lung. N Engl J Med 1986;315:1377–81.
81. Van Houtte P, Rocmans P, Smets P, et al. Postoperative radiation therapy in lung cancer: a controlled trial after resection of curative design. Int J Radiat Oncol Biol Phys 1980;6:983–6.
82. Israel L, Bonadonna G, Sylvester R, et al. EORTC Lung Cancer Group: controlled study with adjuvant radiotherapy, chemotherapy, immunotherapy and chemoimmunotherapy in operable squamous cell carcinoma of the lung. In: Muggia F, Rozencweig M, eds. Lung cancer: progress in therapeutic research. New York: Raven, 1979:443–52.
83. Green N, Kurohara SS, George FW, Crews QE. Postresection irradiation for primary lung cancer. Radiology 1975,116: 405–7.
84. Chung CK, Stryker JA, O'Neill M Jr, DeMuth WE Jr. Evaluation of adjuvant postoperative radiotherapy for lung cancer. Int J Radiat Oncol Biol Phys 1982;8:1877–80.
85. Astudillo J, Conill C. Role of postoperative radiation therapy in stage IIIa non–small cell lung cancer. Ann Thorac Surg 1990;50:618–23.
86. Holmes EC, Gail M for the Lung Cancer Study Group. Surgical adjuvant therapy for stage II and III adenocarcinoma and large-cell undifferentiated carcinoma. J Clin Oncol 1986;4:710–5.
87. Lad T, Rubinstein L, Sadeghi A for the Lung Cancer Study Group. The benefit of adjuvant treatment for resected locally advanced non–small cell lung cancer. J Clin Oncol 1988;6:9–17.
88. Thomas P, Feld R, Lung Cancer Study Group. Preliminary report of a clinical trial comparing post resection adjuvant chemotherapy versus no therapy for T1N1,T2N0 non small cell lung cancer [Abstract]. Lung Cancer 1988;4(Suppl): A160.
89. Warram J. A collaborative study: preoperative irradiation of cancer of the lung: final report of a therapeutic trial. Cancer 1975;36:914–25.
90. Shields TW. Preoperative radiation therapy in the treatment of bronchial carcinoma. Cancer 1972;30:1388–94.
91. Reddy S, Faber LP, Baumann LA, et al. Preoperative radiation therapy in regionally stage III non–small cell lung carcinoma: long term results and patterns of failure. Int J Radiat Oncol Biol Phys 1990;19:287–92.
92. Strauss G, Sherman D, Schwartz J, et al. Combined modality treatment for regionally advanced stage III non–small cell carcinoma of the lung (NSCLC) employing neoadjuvant chemotherapy (CT), radiotherapy (RT), and surgery (S) [Abstract]. Proc Am Soc Clin Oncol 1986;5:172.
93. Eagan RT, Ruud C, Lee RE, et al. Pilot study of induction therapy with cyclophosphamide, doxorubicin, and cisplatin (CAP) and chest irradiation prior to thoracotomy in initially

inoperable stage IIIM0 non–small cell lung cancer. Cancer Treat Rep 1987;71:895–900.

94. Strauss G, Sherman L, Matthiesen O, et al. Concurrent chemotherapy and radiotherapy followed by surgery in marginally resectable stage IIIa non–small cell lung cancer: a Cancer and Acute Leukemia Group B study [Abstract]. Proc Am Soc Clin Oncol 1988;7:203.
95. Skarin A, Jochelson M, Sheldon T, et al. Neoadjuvant chemotherapy in marginally resectable stage IIIM0 non–small cell lung cancer: long-term follow-up in 41 patients. J Surg Oncol 1989;40:266–74.
96. Elias AD, Skarin AT, Socinski MA, et al. Neoadjuvant therapy for stage IIIa non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1989;8:241.
97. Elias AD, Skarin AT, Socinski MA, et al. Neoadjuvant therapy for unresectable stage IIIb non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1989; 8:242.
98. Faber LP, Kittle CF, Warren WH, et al. Preoperative chemotherapy and irradiation for stage III non–small cell lung cancer. Ann Thorac Surg 1989;47:669–77.
99. Henriquez I, Munoz-Galindo L, Rebollo J, et al. Neoadjuvant chemotherapy (NAC) with cisplatin (CDDP), mitomycin-C (MMC) and vindesine (VDS) in locally advanced non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1990;9:227.
100. Weitberg A, Posner M, Yashar J, et al. Combined modality therapy for stage IIIa non–small cell carcinoma of the lung (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1990;9:226.
101. Albain K, Rusch V, Crowley J, et al. Concurrent cisplatin (DDP), VP-16, and chest irradiation (RT) followed by surgery for stages IIIa and IIIb non–small cell lung cancer (NSCLC): a Southwest Oncology (SWOG) study (#8805) [Abstract]. Proc Am Soc Clin Oncol 1991;10:244.
102. Ellis E, Vokes E, Hoffman P, et al. A phase II study of neoadjuvant chemotherapy (NC) and concomitant chemoradiotherapy (CCRT) for stage III non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1991;10:267.
103. Fowler WC, Langer CJ, Keller SM, et al. Morbidity and mortality of pneumonectomy following concurrent chemotherapy (5-fluorouracil, cisplatin, etoposide) and high-dose thoracic radiation (RT) for locally advanced non–small cell lung cancer [Abstract]. Proc Am Soc Clin Oncol 1991;10:255.
104. Rebischung JL, Vannetzel JM, Darteville P, Chapelier A, GEARC. Cyclic concomitant chemo-radiotherapy (CCCR) for primary inoperable non small cell lung cancer (INSCLC) [Abstract]. Proc Am Soc Clin Oncol 1991;10:254.
105. Bedini AV, Tavecchio L, Milani F, et al. Prolonged venous infusion of cisplatin and concurrent radiation therapy for lung carcinoma. A feasibility study. Cancer 1991;67:357–62.
106. Weiden PL, Piantadosi S, Lung Cancer Study Group. Preoperative chemotherapy (cisplatin and fluorouracil) and radiation therapy in stage III non–small-cell lung cancer: a phase II study of the Lung Cancer Study Group. J Natl Cancer Inst 1991;83:266–73.
107. Folman R, Rosman M, Auerbach S. Mitomycin-C, vinblastine and cis-platinum (MVP) in the combined modality treatment of non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1984;3:232.
108. Takita H, Regal A-M, Antkowiak JG, et al. Chemotherapy followed by lung resection in inoperable non–small cell lung carcinomas due to locally far-advanced disease. Cancer 1986;57:630–5.
109. Sridhar KS, Thurer R, Kim Y, et al. Multimodality treatment of non–small cell lung cancer: response to cisplatin, VP-16, and 5-FU chemotherapy and to surgery and radiation therapy. J Surg Oncol 1988;38:193–215.
110. Spain RC. Neoadjuvant mitomycin C, cisplatin, and infusion vinblastine in locally and regionally advanced non–small cell lung cancer: problems and progress from the perspective of long-term follow-up. Semin Oncol 1988;15: 6–15.
111. Burkes R, Ginsberg R, Shepherd F, et al. Neo-adjuvant trial with MVP (mitomycin-C + vindesine + cisplatin) chemotherapy for stage III (T1–3, N2 M0) unresectable non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1989;8:221.
112. Vokes EE, Bitran JD, Hoffman PC, et al. Neoadjuvant vindesine, etoposide, and cisplatin for locally advanced non–small cell lung cancer. Final report of a phase II study. Chest 1989;96:110–3.
113. Pisters KMW, Kris MG, Gralla RJ, Martini N. Preoperative chemotherapy in stage IIIa non–small cell lung cancer: an analysis of a trial in patients with clinically apparent mediastinal node involvement. In: Salmon SE, ed. Adjuvant therapy of cancer VI, Proceedings of the sixth international conference on the adjuvant therapy of cancer. Philadelphia: Saunders, 1990:133–7.
114. Chapman R, Lewis O, Kvale P, et al. A neoadjuvant trial in stage II and IIIa non–small cell lung cancer with cisplatin and vinblastine chemotherapy [Abstract]. Proc Am Soc Clin Oncol 1990;9:246.
115. Lad T, Wagner H, Piantadosi S for the Lung Cancer Study Group. Randomized phase II evaluation of pre-operative chemotherapy alone and radiotherapy alone in stage IIIa non–small cell lung cancer [Abstract]. Proc Am Soc Clin Oncol 1991;10:258.
116. Fossella FV, Ryan B, Dhingra H, et al. Interim report of a prospective randomized trial of neoadjuvant chemotherapy plus surgery versus surgery alone for stage IIIa non–small cell lung cancer (NSCLC) [Abstract]. Proc Am Soc Clin Oncol 1991;10:240.
117. Perez CA, Stanley K, Rubin P, et al. A prospective randomized study of various irradiation doses and fractionation schedules in the treatment of inoperable non–oat-cell carcinoma of the lung. Preliminary report by the Radiation Therapy Oncology Group. Cancer 1980;45:2744–53.
118. Cox JD, Azarnia N, Byhardt RW, et al. A randomised phase I/II trial of hyperfractionated radiation therapy with total doses of 60.0 Gy to 79.2 Gy: possible survival benefit with ≥ 69.9 Gy in favorable patients with Radiation Therapy Oncology Group stage III non–small cell lung carcinoma: report of Radiation Therapy Oncology Group 83-11. J Clin Oncol 1990;8:1543–55.
119. Green MR. Unresectable stage III non–small cell lung cancer: lessons and directions from clinical trials research [Editorial]. J Natl Cancer Inst 1991;83:382–3.
120. Schaake-Koning C, Maat B, Van Houtte P, et al. Radiotherapy combined with low-dose cis-diammine dichloroplatinum (II) (CDDP) in inoperable nonmetastatic non–small cell lung cancer (NSCLC): a randomized three arm phase II study of the EORTC lung cancer and Radiotherapy Cooperative Groups. Int J Radiat Oncol Biol Phys 1990;19:967–72.
121. Dillman RO, Seagren SL, Propert KJ, et al. A randomized trial of induction chemotherapy plus high-dose radiation versus radiation alone in stage III non–small cell lung cancer. N Engl J Med 1990;323:940–5.
122. Cox JD, Azarnia N, Byhardt RW, et al. N2 (clinical) non–small cell carcinoma of the lung: prospective trials of radiation therapy with total doses 60 Gy by the Radiation Therapy Oncology Group. Int J Radiat Oncol Biol Phys 1991;20:7–12.
123. Bonomi P, Reddy S, Faber LP. Concurrent chemotherapy and thoracic irradiation in non–small cell lung cancer. Hemat Oncol Clin North Am 1990;4:1143–58.
124. Deslauriers J. Discussion of: Jensik RJ, Faber LP, Kittle CF, Miley RW, Thatcher WC, El-Baz N. Survival in patients undergoing tracheal sleeve pneumonectomy for bronchogenic carcinoma. J Thorac Cardiovasc Surg 1982;84:489–96.
125. Fujimura S, Kondo T, Imai T, et al. Prognostic evaluation of tracheobronchial reconstruction for bronchogenic carcinoma. J Thorac Cardiovasc Surg 1985;90:161–6.
126. Dartevelle PG, Khalife J, Chapelier A, et al. Tracheal sleeve pneumonectomy for bronchogenic carcinoma: report of 55 cases. Ann Thorac Surg 1988;46:68–72.
127. Mastrorilli M, Bragaglia RB, Cippola D'Abruzzo G, et al.

The tracheo-bronchoplastic procedures for lung cancer [Abstract]. Lung Cancer 1988;4(Suppl):A87.
128. Tsuchiya R, Goya T, Naruke T, Suemasu K. Resection of tracheal carina for lung cancer. J Thorac Cardiovasc Surg 1991;99:779–87.
129. Vogt-Moykopf I, Meyer G, Naunheim K, et al. In: Baue AE, Geha AS, Hammond GL, Luks H, Naunheim KS, eds. Glenn's thoracic and cardiovascular surgery. 5th ed. East Norwalk, CT: Appleton & Lange, 1991:403–17.
130. Mathisen DJ, Grillo HC. Carinal resection for bronchogenic cancer. J Thorac Cardiovasc Surg 1991;102:16–23.
131. Darteville P, Chapelier A, Navajas M, et al. Replacement of the superior vena cava with polytetrafluoroethylene grafts combined with resection of mediastinal–pulmonary malignant tumors. J Thorac Cardiovasc Surg 1987;94:361–6.
132. Nakahara K, Ohno K, Mastumura A, et al. Extended operation for lung cancer invading the aortic arch and superior vena cava. J Thorac Cardiovasc Surg 1989;97:428–33.
133. Inoue H, Shohtsu A, Koide S, et al. Resection of the superior vena cava for primary lung cancer: 5 years' survival. Ann Thorac Surg 1990;50:661–2.
134. DeMeester TR, Albertucci M, Dawson PJ, Montner SM. Management of tumor adherent to the vertebral body. J Thorac Cardiovasc Surg 1989;97:373–8.
135. Parker EF. Discussion of: Martini N, Flehinger BJ, Zaman MB, Beattie EJ Jr. Prospective study of 445 lung carcinomas with mediastinal lymph node metastases. J Thorac Cardiovasc Surg 1980;80:390–9.
136. Martini N, McCormack P. Therapy of stage III (nonmetastatic) disease. Semin Surg Oncol 1983;10:95–110.
137. Decker DA, Dines DE, Payne WS, et al. The significance of a cytologically negative pleural effusion in bronchogenic carcinoma. Chest 1978;6:640–2.
138. Reyes L, Parvez Z, Regal AM, Takita H. Neoadjuvant chemotherapy and operations in the treatment of lung cancer with pleural effusion [Letter]. J Thorac Cardiovasc Surg 1991;101:946–7.
139. Canto A, Ferrer G, Romagosa V, et al. Lung cancer and pleural effusion: clinical significance and study of pleural metastatic locations. Chest 1985;87:649–52.
140. Thomas P. Thoracoscopy: an old procedure revisited. In: Kittle CF, ed. Current controversies in thoracic surgery. Philadelphia: Saunders, 1986:101–6.
141. Kaiser LR. Diagnostic and therapeutic uses of pleuroscopy (thoracoscopy) in lung cancer. Surg Clin North Am 1987;67:1081–6.
142. Naruke T, Goya T, Tsuchiya R, Suemasu K. Extended radical operation for N2 left lung cancer through median sternotomy [Abstract]. Lung Cancer 1988;4(Suppl):A89.
143. Hata E, Hayakawa K, Miyamoto H, et al. The incidence and the prognosis of the contralateral mediastinal node involvement of the left lung cancer patients who underwent bilateral mediastinal dissection and pulmonary resection through a median sternotomy [Abstract]. Lung Cancer 1988;4(Suppl):A87.
144. Watanabe Y, Ichihashi T, Iwa T. Median sternotomy as an approach for pulmonary surgery. Thorac Cardiovasc Surg 1988;36:227–31.
145. Ferguson MK. Diagnosing and staging of non–small cell lung cancer. Hemat Oncol Clin North Am 1990;4:1053–68.
146. Stanley KE. Prognostic factors for survival in patients with inoperable lung cancer. J Natl Cancer Inst 1980;65:25–32.
147. Lanzotti VJ, Thomas DR, Boyle L, et al. Survival with inoperable lung cancer. Cancer 1977;39:303–13.
148. O'Connell JP, Kris MG, Gralla RJ, et al. Frequency and prognostic importance of pretreatment clinical characteristics in patients with advanced non–small cell lung cancer treated with combination chemotherapy. J Clin Oncol 1986;4:1604–14.
149. Bitran JD, Vokes EE. Chemotherapy for stage IV non–small cell lung cancer. Hemat Oncol Clin North Am 1990;4:1159–68.
150. Rapp E, Pater JL, Willan A. Chemotherapy can prolong survival in patients with advanced non–small cell lung cancer: report of a Canadian multicenter trial. J Clin Oncol 1988;6:633–41.
151. Awan AM, Weichselbaum RR. Palliative radiotherapy. Hemat Oncol Clin North Am 1990;4:1169–81.
152. Kaiser LR. Management of tracheobronchial lesions with the Nd-YAG laser. Surg Clin North Am 1987;67:1087–92.
153. Pairolero PC, Williams DE, Bergstralh EJ, Piehler JM, Bernatz PE, Payne WS. Postsurgical stage I bronchogenic carcinoma: morbid implications of recurrent disease. Ann Thorac Surg 1984;38:331–8.
154. Immerman SC, Vanecko RM, Fry WA, Head LR, Shields TW. Site of recurrence in patients with stage I and II carcinoma of the lung resected for cure. Ann Thorac Surg 1981;32:23–7.
155. Rosengart TK, Martini N, Ghosn P, Burt M. Multiple primary lung carcinomas: prognosis and treatment. Ann Thorac Surg 1991;52:773–9.
156. Jensik RJ, Faber LP, Kittle CF, Meng RL. Survival following resection for second primary bronchogenic carcinoma. J Thorac Cardiovasc Surg 1981;82:658–68.
157. Mathisen DJ, Jensik RJ, Faber LP, Kittle CF. Survival following resection for second and third primary lung cancers. J Thorac Cardiovasc Surg 1984;88:502–10.
158. Martini N, Melamed MR. Multiple primary lung cancers. J Thorac Cardiovasc Surg 1975;70:606–12.
159. Ferguson MK, De Meester TR, Deslauriers J, et al. Diagnosis and management of synchronous lung cancers. J Thorac Cardiovasc Surg 1985;89:378–85.
160. Deslauriers J, Brisson J, Cartier R, et al. Carcinoma of the lung: evaluation of satellite nodules as a factor influencing prognosis after resection. J Thorac Cardiovasc Surg 1989;97:504–12.
161. McCormack P. Surgical resection of pulmonary metastasis. Semin Surg Oncol 1990;6:297–302.
162. Magilligan DJ, Duvernoy C, Malik G, et al. Surgical approach to lung cancer with solitary cerebral metastasis: twenty-five years' experience. Ann Thorac Surg 1986;42:360–4.
163. Figlin RA, Piantadosi S, Feld R, Lung Cancer Study Group. Intracranial recurrence of carcinoma after complete surgical resection of stage I, II, and III non–small cell lung cancer. N Engl J Med 1988;318:1300–5.
164. Delattre JY, Krol G, Thaler HT, Posner JB. Distribution of brain metastases. Arch Neurol 1988;45:741–4.
165. Martini N. Rationale for surgical treatment of brain metastasis in non–small cell lung cancer. Ann Thorac Surg 1986;42:357–8.
166. Salerno TA, Little JR, Munro DD. Bronchogenic carcinoma with a brain metastasis: a continuing challenge. Ann Thorac Surg 1979;27:235–7.
167. Winston KR, Walsh JW, Fischer EG. Results of operative treatment of intracranial metastatic tumors. Cancer 1980;45:2639–45.
168. White KT, Fleming TR, Laws ER. Single metastasis to the brain: surgical treatment in 122 consecutive patients. Mayo Clin Proc 1981;56:424–8.
169. Deviri E, Schachner A, Halevy A, Shalit M, Levy MJ. Carcinoma of the lung with a solitary cerebral metastasis: surgical management and review of the literature. Cancer 1983;52:1507–9.
170. Yardeni D, Reichenthal E, Zücker G, et al. Neurosurgical management of single brain metastasis. Surg Neurol 1984;21:377–84.
171. Mussi A, Janni A, Pistolesi M, et al. Surgical treatment of primary lung cancer and solitary brain metastasis. Thorax 1985;40:191–3.
172. Tummarello D, Porfiri E, Rychlicki F, et al. Non–small cell lung cancer: neuroresection of the solitary intracranial metastasis followed by radiochemotherapy. Cancer 1985;56:2569–72.
173. Fry WA. Discussion of: Magilligan DJ, Duvernoy C, Malik

G, et al. Surgical approach to lung cancer with solitary cerebral metastasis: twenty-five years' experience. Ann Thorac Surg 1986;42:360–4.

174. Ehrenhaft JL. Discussion of: Magilligan DJ, Duvernoy C, Malik G, et al. Surgical approach to lung cancer with solitary cerebral metastasis: twenty-five years' experience. Ann Thorac Surg 1986;42:360–4.
175. Hankins JR, Miller JE, Salcman M, et al. Surgical management of lung cancer with solitary cerebral metastasis. Ann Thorac Surg 1988;46:24–8.
176. Torre M, Quaini E, Chiesa G, et al. Synchronous brain metastasis from lung cancer: results of surgical treatment in combined resection. J Thorac Cardiovasc Surg 1988;95:994–7.
177. Catinella FP, Kittle CF, Faber LP, et al. Surgical treatment of primary lung cancer and solitary intracranial metastasis. Chest 1989;95:972–5.
178. Read RC, Boop WC, Yoder G, Schaefer R. Management of nonsmall cell lung carcinoma with solitary brain metastasis. J Thorac Cardiovasc Surg 1989;98:884–91.
179. Macchiarini P, Bonaguidi R, Hardin M, Angeletti CA. Results and prognostic factors of surgery in the management of non–small cell lung cancer (NSCLC) with solitary brain metastasis (SBM) [Abstract]. Proc Am Soc Clin Oncol 1991;10:253.
180. Chavantes MC, Zamorano L, Dujovny M, et al. Management of lung cancer with brain metastasis [Abstract]. Proc Am Soc Clin Oncol 1988;7:213.
181. Galicich JH, Sundaresan N, Arbit E, Passe S. Surgical treatment of single brain metastasis: factors associated with survival. Cancer 1980;45:381–6.
182. Sundaresan N, Galicich JH. Surgical treatment of single brain metastases from non–small cell lung cancer. Cancer Invest 1985;3:107–13.
183. Burt M, Wronski M, Galicich J, Martini N, Ginsberg R, Members of the Memorial Sloan-Kettering Cancer Center Thoracic and Neurosurgical Services. Solitary brain metastasis from non–small cell lung cancer: results of therapy. Presented at the 71st Annual Meeting of the American Association for Thoracic Surgery, Washington, DC, May 6–8, 1991.
184. Patchell RA, Tibbs PA, Walsh JW, et al. A randomized trial of surgery in the treatment of single metastases to the brain. N Engl J Med 1990;322:494–500.
185. Sandler MA, Paerlberg JL, Madrazo BL, et al. Computed tomographic evaluation of the adrenal gland in the preoperative assessment of bronchogenic carcinoma. Radiology 1982;145:733–6.
186. Nielsen ME Jr, Heaston DK, Dunnick NR, Korobkin M. Preoperative CT evaluation of adrenal glands in non–small cell bronchogenic carcinoma. AJR 1982;139:317–20.
187. Allard P, Yankaskas BC, Fletcher RH, et al. Sensitivity and specificity of computed tomography for the detection of adrenal metastatic lesions among 91 autopsied lung cancer patients. Cancer 1990;66:457–62.
188. Twomey P, Montgomery C, Clark O. Successful treatment of adrenal metastasis from large-cell carcinoma of the lung. JAMA 1982;248:581–3.
189. Raviv G, Klein E, Yellin A, et al. Surgical treatment of solitary adrenal metastases from lung carcinoma. J Surg Oncol 1990;43:123–4.
190. Reyes L, Parvez Z, Nemoto T, et al. Adrenalectomy for adrenal metastasis from lung carcinoma. J Surg Oncol 1990;44:32–4.
191. Deslauriers J, Ginsberg RJ, Dubois P, et al. Current operative morbidity associated with elective surgical resection for lung cancer. Can J Surg 1989;32:335–9.

Aortic Valve Repair

Delos M. Cosgrove III, MD

The Cleveland Clinic Foundation, Cleveland, Ohio

Anatomy and Pathology of the Aortic Valve

1. Davies MJ. Pathology of cardiac valves. London: Butterworths, 1980:172.
2. Moore GW, Hutchins GM, Brito JC, Kang H. Congenital malformations of the semilunar valves. Hum Pathol 1980;11:367–72.
3. Olson LJ, Subramanian R, Edwards WD. Surgical pathology of pure aortic insufficiency. A study of 225 cases. Mayo Clin Proc 1984;59:835–41.
4. Passik CS, Ackermann DM, Pluth JR, Edwards WD. Temporal changes in the causes of aortic stenosis. A surgical pathologic study of 646 cases. Mayo Clin Proc 1987;62:119–23.
5. Subramanian R, Olson LJ, Edwards WD. Surgical pathology of pure aortic stenosis. A study of 374 cases. Mayo Clin Proc 1984;59:683–90.
6. Sud A, Parker F, Magilligan DJ. Anatomy of the aortic root. Ann Thorac Surg 1984;38:76–80.
7. Thubrikar M. The aortic valve. Boca Raton: CRC Press, 1990:211.

Stenosis

Congenital Valvar

8. Leung MP, McKay R, Smith A, Anderson RH, Arnold R. Critical aortic stenosis in early infancy, anatomic and echocardiographic substrates of successful open valvotomy. J Thorac Cardiovasc Surg 1991;101:526–35.
9. Rhodes LA, Colan SD, Perry SB, Jonas RA, Sanders SP. Predictors of survival in neonates with critical aortic stenosis. Circulation 1991;84:2325–35.
10. Wheller JJ, Hosier DM, Teske DW, Craenen JM, Kilman JW. Results of operation for aortic valve stenosis in infants, children, and adolescents. J Thorac Cardiovasc Surg 1988;96:474–7.
11. Zeevi B, Keane JF, Castaneda AR, Perry SB, Lock JE. Neonatal critical valvar aortic stenosis. A comparison of surgical and balloon dilation therapy. Circulation 1989;80:831–9.

Calcific

12. Brown AH, Davies PGH. Ultrasonic decalcification of calcified cardiac valves and annuli. Br Med J 1972;3:274–7.
13. Cosgrove DM, Ratliff NB, Schaff HV, Edwards WD. Aortic valve decalcification: history repeated with a new result. Ann Thorac Surg 1990;49:689–90.
14. Craver JM. Aortic valve debridement by ultrasonic surgical aspirator: a word of caution. Ann Thorac Surg 1990;49:746–53.
15. Freeman WE, Schaff HV, King RM, Orszulak TA. Ultrasonic aortic valve decalcification: Doppler echocardiographic evaluation [Abstract]. J Am Coll Cardiol 1988;11:229A.
16. Mindich BP, Guarino T, Krenz H, Li XG, Gonzales E. Aortic valve salvage utilizing high frequency vibratory debridement [Abstract]. J Am Coll Cardiol 1988;11:3A.

Insufficiency

Prolapse Associated With a Ventricular Septal Defect

17. Okita Y, Miki S, Kusuhara K, et al. Long-term results of aortic valvuloplasty for aortic regurgitation associated with ventricular septal defect. J Thorac Cardiovasc Surg 1988;96:769–74.
18. Somerville J, Brandao A, Ross DN. Aortic regurgitation with ventricular septal defect: surgical management and clinical features. Circulation 1970;41:317–30.
19. Spencer FC, Doyle EF, Danilowicz DA, Bahnson HT, Weldon CT. Long-term evaluation of aortic valvuloplasty for aortic insufficiency and ventricular septal defect. J Thorac Cardiovasc Surg 1973;65:15–31.
20. Starr A, Menashe V, Dotter D. Surgical correction of aortic insufficiency associated with ventricular septal defect. Surg Gynecol Obstet 1960;111:71–6.
21. Trusler GA, Moes CAF, Kidd BSL. Repair of ventricular septal defect with aortic insufficiency. J Thorac Cardiovasc Surg 1973;66:394–403.
22. Van Praagh R, McNumara JJ. Anatomic types of ventricular septal defect with aortic insufficiency: diagnostic and surgical considerations. Am Heart J 1968;75:604–19.

Prolapse of a Bicuspid Valve

23. Campbell M. Calcific aortic stenosis and congenital bicuspid aortic valves. Br Heart J 1968;30:606.
24. Cosgrove DM, Rosenkranz ER, Hendren WG, Bartlett JC, Stewart WJ. Valvuloplasty for aortic insufficiency. J Thorac Cardiovasc Surg 1991;102:571–7.
25. Mills P, Leech G, Davies M, Leatham A. The natural history of a nonstenotic bicuspid aortic valve. Br Heart J 1978;40:951–7.
26. Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. Am J Cardiol 1970;26:72–83.
27. Roberts WC, Morrow AG, McIntosh CL, Jones M, Epstein SE. Congenitally bicuspid aortic valve causing severe, pure aortic regurgitation without superimposed infective endocarditis. Analysis of 13 patients requiring aortic valve replacement. Am J Cardiol 1981;47:206–9.

Prolapse Secondary to Rupture of a Fenestration

28. Carter JB, Sethi S, Lee GB, Edwards JE. Clinicopathologic correlations: prolapse of semilunar cusps as causes of aortic insufficiency. Circulation 1971;43:922–32.
29. Marcus FI, Ronan J, Misanik LF, Ewy GA. Aortic insufficiency secondary to spontaneous rupture of a fenestrated leaflet. Am Heart J 1963;66:675–8.
30. Moran SV, Casanegra P, Maturana G, Dubernet J. Spontaneous rupture of a fenestrated aortic valve: surgical treatment. J Thorac Cardiovasc Surg 1977;73:716–8.

Annular Dilatation

31. Carpentier A. Cardiac valve surgery—the "French correction." J Thorac Cardiovasc Surg 1983;86:323–37.
32. Cabrol C, Guiraudon G, Bertrand M. Le traitement de l'insuffisance aortique par l'annuloplastie aortique. Arch Mal Coeur 1966;59:1305–12.
33. David RE, Feindel CM. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. J Thorac Cardiovasc Surg 1992;103:617–22.

Address reprint requests to Dr Cosgrove, Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:1014–5 • 0003-4975/92/$5.00

34. Duran CG. Reconstructive techniques for rheumatic aortic valve disease. J Cardiac Surg 1988;3:23–8.
35. Frater RWM. Aortic valve insufficiency due to aortic dilatation: correction by sinus rim adjustment. Circulation 1986; 74(Suppl 1):136–42.

Cusp Perforation

36. Denyer MH, Elliott CM, Robicsek F. Pericardial patch repair of aortic cusp perforation caused by cardiac catheterization. J Cardiac Surg 1988;3:155–7.

REVIEW OF RECENT BOOKS

Cardiac and Noncardiac Complications of Open Heart Surgery: Prevention, Diagnosis and Treatment
Edited by Morris N. Kotler, MD, and Anthony Alfieri, DO
Mount Kisco, NY, Futura Publishing Company, 1992
418 pp, illustrated, $62.00

Reviewed by James L. Nielsen, MD

With this book, the editors provide the nonsurgeon a basic framework for the management of complications following cardiac operations. Although the book was written by cardiologists for cardiologists, surgical house staff and those in cardiac surgery training may also find it a useful reference.

This work begins with a chapter on the cardiologist's perspective of coronary bypass operations, and includes a thorough literature review of the indications for coronary artery bypass. The author also makes a point of the lack of rigorously controlled studies comparing coronary angioplasty with bypass operation.

The next four chapters focus on specific postoperative cardiac problems, with discussions of the interpretation of electrocardiograms and management of arrhythmias. Notable shortcomings in this section are the inadequate coverage of postoperative bleeding, management of early tamponade, and cardiac assist devices.

Progressing into discussion of specific organ system problems, the topics of pulmonary, neurologic, and renal complications and their management are covered in a practical, clinically useful fashion. However, the chapter on gastrointestinal complications tends to spend too much time on etiology and too little on diagnosis and management. Also, in the endocrinology chapter, disproportionate emphasis is placed on rare occurrences such as pituitary apoplexy and adrenal insufficiency.

An in-depth discussion of the prevention of atherosclerotic coronary disease brings the book to a close. The author covers the pathophysiology and reviews prevention trials, condensing the topic into a convenient management algorithm, which includes lifestyle and dietary modifications as well as medications.

Although the editors do not actually say so in their preface, this book is intended for cardiologists taking care of cardiac surgery patients. However, surgeons in training may find it a practical guide for certain problems in their postoperative management.

San Antonio, Texas

The acquisition of new knowledge in thoracic surgery is a continuum. Ideas and practices may change significantly as a result of experience, but there have been limited ways to communicate easily the reasons for such modifications.

The purpose of this section is to present brief follow-up reports from authors whose work was previously published in The Annals of Thoracic Surgery. *The goal is to learn whether the original conclusions have stood the test of time, and whether or not previously recommended techniques have been modified, replaced, or discarded. Contributions to* Update *are short progress reports that do not preclude subsequent more complete articles.*

Thomas B. Ferguson, MD, Editor
John R. Benfield, MD, Associate Editor

1985: A Method for Predicting Postoperative Lung Function and Its Relation to Postoperative Complications in Patients with Lung Cancer

Kazuya Nakahara, M.D., Yasumasa Monden, M.D., Kiyoshi Ohno, M.D.,
Shinichiro Miyoshi, M.D., Hajime Maeda, M.D.,
and Yasunaru Kawashima, M.D.

ABSTRACT We predicted the postoperative forced expiratory volume in 1 second (FEV$_1$) with a formula based on the premise that the total number of subsegments was 42: postop FEV$_1$ = [1 − (b − n)/(42 − n)] (preop FEV$_1$), where n and b are the number of obstructed subsegments and total subsegments, respectively, in the resected lobe. It was assumed that b was 6, 4, and 12 in the right upper, middle, and lower lobes, respectively, and 10 each in the left upper and the left lower lobes. The obstructed subsegments, n, were obtained from the findings on bronchography or bronchofiberscopy or both before operation. The linear regression line derived from the correlation between predicted (x) and measured (y) FEV$_1$ was $y = 0.850x + 0.286 \pm 0.296$ (standard error) ($N = 52$; $r = 0.821$; $p < 0.001$).

We calculated the predicted postoperative FEV$_1$ in 188 patients with primary lung cancer. The predicted values were corrected with the regression equation just mentioned and then normalized by the patient's height and sex (%FEV$_{1(p,c)}$). The correlation between %FEV$_{1(p,c)}$ and the surgical risk was studied. Postoperative respiratory complications were inversely related to %FEV$_{1(p,c)}$, and a significantly high incidence of complications ($p < 0.05$) was observed in those whose %FEV$_{1(p,c)}$ was less than 60% of predicted normal. In aged patients (65 years old or more) without complications, %FEV$_{1(p,c)}$ was 67.3 ± 18.0%; it was 52.2 ± 12.8% in those with respiratory trouble and 53.3% ± 9.6% in those with circulatory complications. The difference between groups with and without complications was significant ($p < 0.01$). In the nonaged group, there were no significant differences among the patients with no complications, respiratory complications, or circulatory complications.

We conclude that our formula involving subsegments is a reliable method for predicting postoperative lung function and is a predictor of the surgical risk in aged patients with lung cancer.

1992 Update: Kazuya Nakahara, MD, Shinichiro Miyoshi, MD, and Katuhiro Nakagawa, MD

First Department of Surgery, Osaka University Medical School, Osaka, Japan

At present evaluation of the predicted postoperative function [1] is a routine procedure to identify functionally poor patients. Preoperative physiotherapies such as IPPB with a bronchodilator, incentive spirometry, and exercise loading are adopted for such patients. However the effectiveness of such therapies is still inconclusive, and the postoperative complication rate is still at the same level as in the previous report. Although thoracotomy is not feasible in patients with a %VC$_{(p,\,c)}$ less than 40% and a %FEV$_{1.0\,(p,\,c)}$ less than 30%, these parameters do not predict the ability or inability of patients to recover from complications [2]. Adopting an incremental exercise test by bicycle ergometer, we found that $\dot{V}O_2$ at an arterial

---

Address reprint requests to Dr Nakahara, First Department of Surgery, Osaka University Medical School, 1-1-50, Fukushima, Fukushima-ku, 553, Osaka, Japan.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:1016–7 • 0003-4975/92/$5.00

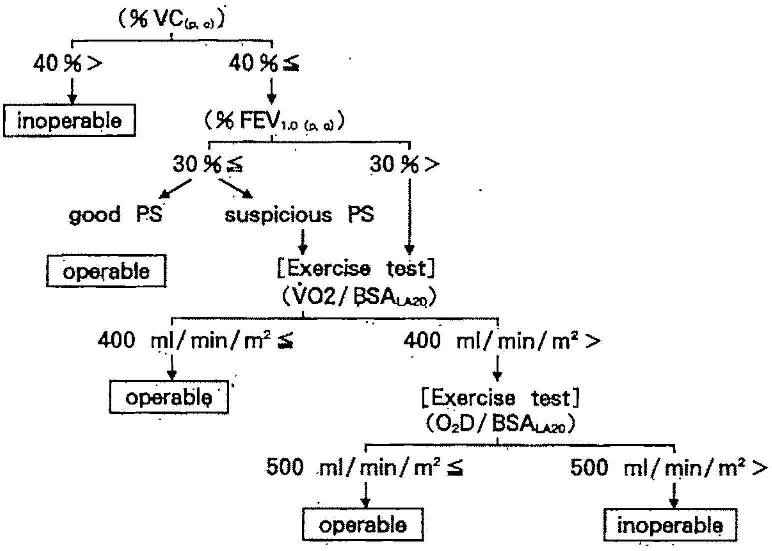


Fig 1. A new guideline for functional evaluation of preoperative patients with lung cancer. (O_2D = *oxygen delivery;* PS = *performance status;* $\dot{V}O2/BSA_{LA20}$ = *oxygen consumption per unit of body surface area at an arterial lactate level of 20 mg/dL;* $\%FEV_{1.0\ (p,c)}$ = *predicted postoperative forced expiratory volume in 1 second over normal value;* %VC = *predicted postoperative vital capacity over normal value.)*

lactate level of 20 mg/dL ($\dot{V}O_2/BSA_{LA20}$) as an "empirical anaerobic threshold" [3] and the oxygen delivery (oxygen delivery = CI × CaO_2) at this lactate level during exercise [4] are good predictors of survival or death for patients due to postoperative complications. We think the evaluation of predicted postoperative pulmonary function presented in the 1985 issue [1] is fundamental to identify poor-risk patients after thoracotomy, for whom an exercise test should be indicated to reach a final decision of whether or not to perform thoracotomy (Fig 1). We have not experienced an operative death after thoracotomy since 1990. A prospective study following this guideline is now being conducted.

References

1. Nakahara K, Monden Y, Ohno K, Miyoshi S, Maeda H, Kawashima Y. A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer. Ann Thorac Surg 1985;39:260–5.
2. Nakahara K, Ohno K, Hashimoto J, et al. Prediction of postoperative respiratory failure in patients undergoing lung resection for lung cancer. Ann Thorac Surg 1988;46:549–52.
3. Miyoshi S. Nakahara K, Ohno K, Monden Y, Kawashima Y. Exercise tolerance test in lung cancer patients: the relationship between exercise capacity and postthoracotomy hospital death. Ann Thorac Surg 1987;44:487–90.
4. Nakagawa K, Nakahara K, Miyoshi S, Kawashima Y. Oxygen transport during incremental exercise load as a predictor of operative risk of lung cancer patients. Chest 1992;101:1369–75.

CORRESPONDENCE

Aprotinin Treatment During Open Heart Operation in a Patient With Severe Thrombocytopenia

To the Editor:

Platelet dysfunction may lead to severe intraoperative and postoperative bleeding in patients requiring open heart operations [1]. In this context severe thrombocytopenia is considered to be particularly hazardous. Recent reports have shown that aprotinin (Trasylol; Bayer AG, Leverkusen, Germany) significantly reduces bleeding after cardiopulmonary bypass [2–4]. We report a case of a patient with extreme thrombocytopenia as a result of graft versus host reaction after bone marrow transplantation undergoing an open heart operation with a minimal amount of bleeding.

A 33-year-old woman was found to suffer from acute myeloblastic leukemia after massive postpartum bleeding 6 months previously. Full remission was achieved by chemotherapy, and she underwent bone marrow transplantation 4 months later. The posttransplantation course was complicated by transient gram-negative bacteremia, which was treated successfully, graft versus host reaction treated by steroids, and the development of venoocclusive liver disease.

A month after the transplantation the Hickman catheter that had been inserted at the time of bone marrow transplantation became infected with coagulase-positive *Staphylococcus*. Because vancomycin treatment failed to control the infection the catheter was removed 9 days later.

During the next 2 weeks her condition deteriorated progressively. Despite antibiotic treatment with vancomycin and rifampin the septicemia could not be controlled; liver and renal function deteriorated and platelet counts decreased progressively. An echocardiographic examination including transesophageal scanning had results suggestive of two intracardiac masses, one within the left ventricle and the other within the right atrium. As these masses were suspected of being infected thrombi, streptokinase treatment was administered with no result. Four days later, because the patient was still septic and deteriorating rapidly, it was decided to explore the heart in the hope that removal of intracardiac infected thrombi would lead to control of her sepsis.

Before the operation her blood test results were as follows (normal values are in parentheses): γ-glutamyl transferase, 370 U (0 to 40 U); alkaline phosphatase, 835 U (60 to 170 U); aspartate aminotransferase, 92 U (7 to 40 U); albumin, 27 g/L (35 to 50 g/L); total proteins, 41 g/L (60 to 80 g/L); urea, 12.6 mmol/L (3.3 to 6.5 mmol/L); total bilirubin, 705 μmol/L (2.5 to 17 μmol/L); white blood cells, 3,500/μL; hemoglobin, 9.4 g/L; thrombocytes, 13,000/μL despite repeated platelet transfusion; and prothrombin time, 70%.

At operation, with the heart arrested using warm blood cardioplegia, all four cardiac chambers were explored. In the left ventricle an abnormally hypertrophied papillary muscle was found, which probably explains the left ventricular echogenic shadow, and the right atrium was free of any mass (possibly false-positive echocardiographic finding). During the operation aprotinine was given before and during cardiopulmonary bypass (total dose of 5×10^6 U). As soon as cardiopulmonary bypass was terminated 6 U of single donor platelets and 1 U of fresh frozen plasma were given. The immediate postoperative course was uneventful. Blood loss was minimal, totalling less than 100 mL in the 24 hours following operation.

The patient was extubated on the day after the operation and the chest drains were removed. Her platelet count, which was 127,000/μL after the operation, fell to 54,000/μL within 48 hours. Three days after the operation the patient became septic again and her blood cultures revealed the same coagulase-positive *Staphylococcus*. Notwithstanding antibiotic treatment including vancomycin, rifampin and fusidic acid, she died on the tenth postoperative day of ongoing sepsis and progressive liver and renal failure. Postmortem examination did not reveal any source of sepsis, and the cardiac chambers and the pulmonary arteries were free of clots.

The prominent feature of this case is the fact that in the presence of severe thrombocytopenia and liver failure the blood loss during and after the operation was minimal. Because the patient received thrombocytes in addition to aprotinin we are unable to conclude that the reason for the lack of bleeding postoperatively was exclusively due to aprotinin. However, the operating field was so dry after bypass that we are convinced that aprotinin played a substantial role in the prevention of severe postoperative bleeding.

Aprotinin has been found to significantly reduce blood loss and the need for homologous blood transfusion after open cardiac operations [4]. Aprotinin is a high molecular weight protease that inhibits the pancreatic enzymes, kallikrein, and plasmin [5]. Its mechanism of action is not fully understood. It is probable that aprotinin inhibits activation of both coagulation and fibrinolysis cascades by the inhibition of plasmin and kallikrein [4, 6, 7]. Even though the number of platelets remains unchanged after aprotinin administration during cardiopulmonary bypass, there is some evidence that it attenuates platelet aggregation and release and the prolongation of bleeding times [4, 7].

Infection of a Hickman catheter in an immunodeficient patient is a well-known complication. In the majority of cases it responds to antibiotic treatment, but occasionally it must be removed [8]. In a few cases infected thrombi may be present within the heart, and surgical removal of the infected thrombi is the only way to control the infection [8, 9].

Despite the very poor general condition of this patient including advanced sepsis and multiorgan failure, she did not show any complication related to her heart operation. The fact that the postoperative bleeding was minimal demonstrates that with the use of aprotinin together with appropriate blood components, open heart operation with acceptable bleeding is possible even in patients with extreme thrombocytopenia.

Ehud Deviri, MD
Uzi Izhar, MD
Benjamin Drenger, MD
Yitzhak Glick, MD
Joseph B. Borman, FRCS(Eng)

Hadassah University Hospital
Cardiothoracic Surgery Department
POB 12000
Jerusalem 91120, Israel

References

1. McKenna R, Bachmann F, Whittaker B, Gilson JR, Weinberg M. The hemostatic mechanism after open-heart surgery: frequency of abnormal platelet function during and after extracorporeal circulation. J Thorac Cardiovasc Surg 1975;70:298–308.
2. Royston D, Taylor KM, Bidstrup BP, Sapsford RN. Effect of aprotinin on need for blood transfusion after repeated open heart surgery. Lancet 1987;1:1289–91.
3. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
4. Blauhut B, Gross C, Necek S, Doran JE, Spath P, Lundsgaard-Hansen P. Effects of high-dose aprotinin on blood loss,

© 1992 by The Society of Thoracic Surgeons

platelet function, fibrinolysis, complement and renal function after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1991; 101:958–67.
5. Royston D. The serine antiprotease aprotinin (Trasylol). A novel approach to reduce postoperative bleeding. Blood Coag Fibrinol 1990;1:55–69.
6. Havel M, Teufelsbauer H, Knobl P, et al. Effect of intraoperative aprotinin administration on postoperative bleeding in patients undergoing cardiopulmonary bypass operation. J Thorac Cardiovasc Surg 1991;101:968–72.
7. Edmunds LH, Niewiarowski S, Colman RW. Aprotinin [Letter]. J Thorac Cardiovasc Surg 1991;101:1103–4.
8. Quinn JP, Counts GW, Meyers JD. Intracardiac infections due to coagulase negative *Staphylococcus* associated with Hickman catheters. Cancer 1986;57:1079–82.
9. Liepman MK, Jones PG, Kauffman CA. Endocarditis as a complication of indwelling right atrial catheters in leukemic patients. Cancer 1984;54:804–7.

Thermo Cardiosystems Left Ventricular Assist Device

To the Editor:

As one of the principal investigators of the HeartMate left ventricular assist device, I would like to comment on the article by Phillips and colleagues [1] that appeared in a recent issue of *The Annals of Thoracic Surgery*. Their report and the following commentary by Hill focus on surgical complications in 3 patients who underwent bridge-to-transplant procedures with the HeartMate. It is important to stress that the complications were related primarily to the operation and, thus, are not a reflection on the suitability and efficacy of the device.

Research on the HeartMate has been ongoing for more than a decade, and our current clinical experience supports its usefulness in providing long-term support for the failing left ventricle [2]. The HeartMate is particularly suitable for patients with chronic congestive heart failure that is characterized primarily by left ventricular failure, a condition in which a heart transplant may also be considered appropriate treatment.

The ultimate use of the HeartMate is not as a bridge to transplantation. The device was originally conceived as a long-term left ventricular assist system, at a time when heart transplantation was not a very successful option. Today, heart transplantation is a successful alternative for patients with end-stage heart failure; unfortunately, many more patients are awaiting a heart transplant than there are available donors. According to the United Network for Organ Sharing [3], an average of fewer than 6 donor hearts are available each day in the United States for more than 2,300 patients who are on the waiting list.

The HeartMate was intended to fill the void left by the shortage of donor hearts and to give patients who are not appropriate candidates for heart transplantation a chance for survival. An intraabdominal device is the only suitable choice for these patients. Our experience has shown that the HeartMate can allow patients to return to active class I cardiac status with minimal limitations, particularly when the newer, electrically powered model is used.

Attributing surgical problems to the device is inappropriate. Intraabdominal or extraperitoneal placement of the HeartMate is a relatively straightforward surgical procedure. Patients appear to tolerate intraabdominal placement well, and in our series there has been only 1 case of intestinal obstruction related to intraabdominal placement. If the goal were simply to provide a bridge to transplantation, an extracorporeal mechanical circulatory assist device could be used and is certainly more convenient for the surgeon to insert and to remove.

We must work toward developing a permanent device, however, as this is one way to treat more patients with terminal heart failure than are currently being treated by heart transplantation. The number of patients awaiting transplants exceeds, by far, the number of potential donors. An extracorporeal device cannot solve the problem caused by too few donors, nor can it be used to provide practical, permanent, implantable cardiac support, which is the only way a patient could live normally with one of these devices. Although an extracorporeal device is simple to implant for the surgeon, this is certainly no justification for its use at a time of critical donor shortage, when a donor heart could just as easily be allocated to a patient waiting for a transplant without a bridging device. Thus, the real goal of bridge-to-transplant procedures must be research that will lead to a clinically practical, permanently implantable device that will allow us to treat a greater number of patients with end-stage heart failure.

O. H. Frazier, MD

Cullen Cardiovascular Research Laboratories
Transplant Service
Texas Heart Institute
PO Box 20345
Houston, TX 77225-0345

References

1. Phillips WS, Burton NA, Macmanus Q, Lefrak EA. Surgical complications in bridging to transplantation: the Thermo Cardiosystems LVAD. Ann Thorac Surg 1992;53:482–6.
2. Frazier OH, Rose E, Macmanus Q, et al. Multicenter clinical evaluation of the HeartMate 1000 IP left ventricular assist device. Ann Thorac Surg 1992;53:1080–90.
3. The National Organ Procurement and Transplantation Network. UNOS Annual Report for January 1, 1990–June 30, 1991. Richmond, VA: UNOS, 1991.

Reply

To the Editor:

We appreciate and concur with the comments of Dr Frazier in response to both our article and the invited comments of Dr Hill. The most important point to emphasize is that in spite of complications, the HeartMate left ventricular assist device provided excellent support in a variety of physiologic conditions without malfunction. Even in the setting of mediastinitis and peritonitis, the device continued to function superbly, and we were able to completely clear the infection while awaiting cardiac transplantation.

We have now used the HeartMate to successfully bridge 8 patients to cardiac transplantation. One patient is currently awaiting transplantation on the device. We agree with Dr Frazier that this device is uniquely adapted for long-term use and will ultimately serve as a substitute for, rather than a bridge to, cardiac transplantation. As Dr Frazier correctly notes, the only mechanical device that will ever alleviate the growing shortage of donor hearts is a device that can be permanently implanted to support a failing left ventricle. Clearly, the first-generation extracorporeal left ventricular assist devices will never allow for such support. By contrast, the intraabdominally placed HeartMate left ventricular assist device has demonstrated to us a remarkable record of dependability and relative freedom from complications. In more than 600 patient-days in our 9 patients, there has never been a single thromboembolic event on a regimen consisting of only 80 mg of aspirin daily. There have been no system failures. All patients have been fully ambulatory and returned to functional class I status.

Although there are potential complications associated with the use of any mechanical device, the HeartMate left ventricular assist device seems to be well-suited for long-term ventricular support. With the next generation of this device, a nontethered vented electric pump, such patients will be able to be fully mobile and return to a nearly normal lifestyle.

Nelson A. Burton, MD
W. Stephen Phillips, MD
Quentin Macmanus, MD
Edward A. Lefrak, MD

3301 Woodburn Rd
Suite 301
Annandale, VA 22003

Plateletpheresis and Transfusion Practice in Heart Operations

To the Editor:

In a recent publication [1] we reported that prebypass plateletpheresis reduced the perioperative use of homologous blood products. One criticism of this study was the small number of patients involved. We commenced plateletpheresis in March 1991. Our experience to date involves more than 450 patients, and we report here the resultant impact on transfusion practice at our institution.

Table 1 shows the average total transfusion requirements per coronary artery bypass graft patient over the past 4 years. This includes primary, redo, elective, and emergency coronary artery bypass grafting. Incidentally, intraoperative autotransfusion was introduced in October 1988.

The blood utilization figures for 1991 include 305 patients who did not have plateletpheresis because they were operated on either on an emergency basis, before the introduction of high-yield pheresis, or by surgeons not using the technique.

Pharmacological reduction of bleeding associated with cardiopulmonary bypass has received much recent attention. The use of antifibrinolytic drugs such as aprotinin holds promise but may prove to be very expensive [2].

A recent study involving 1,480 patients at the Montreal Heart Institute indicated that primary and repeat coronary artery bypass grafting were associated with the use of 5 and 8 units of homologous blood products, respectively [2]. We believe the reduction in our homologous blood product requirements is due to the amelioration of cardiopulmonary bypass–induced coagulopathy brought about by the use of prebypass plateletpheresis.

Table 1. Blood Product Utilization in Coronary Artery Bypass Grafting (including emergency, primary, and repeat procedures)

Year	No. of Patients	RBC	FFP	PLT	CRYO	HBT	HBT/case
1988	328	5.1	0.9	6	1.6	4,495	13.7
1989	410	3.8	0.9	9	3.0	6,929	16.9
1990	467	3.9	1.4	7	0.4	5,978	12.8
1991	552	1.9	0.4	2	0.02	2,499	4.5
3/91–3/92[a]	319	1.6	0.3	0.3	0.01	745	2.3

[a] All patients undergoing coronary artery bypass by the two surgeons using routine plateletpheresis after its introduction in March 1991.

CRYO = cryoprecipitate units per case; HBT = total homologous blood or blood product units used; FFP = fresh frozen plasma units per case; PLT = platelet units per case; RBC = units of packed red blood cells per case.

Gerald G. Davies, FFARCSI
Douglas G. Wells, FFARACS
Richard Sadler, MD
Thomas M. Mabee, MD
Mitchell Ruffcorn, MD
John B. Dooley, MD

St. Luke's Regional Heart Center
1228 E Rusholme
Davenport, IA 52803

References

1. Davies GG, Wells DG, Mabee TM, Sadler R. Platelet-leukocyte plasmapheresis attenuates the deleterious effects of cardiopulmonary bypass. Ann Thorac Surg 1992;53:274–7.
2. Hardy JF, Desroches J. Natural and synthetic antifibrinolytics in cardiac surgery. Can J Anaesth 1992;39:353–65.

Preoperative Morphologic and Physiologic Assessment of Internal Thoracic Arteries

To the Editor:

I read with interest the recent article by Dignan and associates [1] regarding the size and reactivity of the internal thoracic artery (ITA) in elderly patients and women. Using a strain-gauge transducer model, they determined that the contractility and sensitivity of ITA smooth muscle to various vasoconstrictors and vasodilators are not different in elderly and female patients. The question asked by Dr Frederick L. Grover of Denver, CO, in the discussion of this article regarding the correlation of ITA reactivity with diabetes and the response of Dr Dignan stating that they did not look for this correlation prompted me to share our experience on this issue.

In general, there is a reluctance to use ITA grafts in elderly (greater than 70 years) and diabetic patients because of increased risk of surgical complications and death not infrequently related to sternal infections. Furthermore, it is difficult to discern whether an ITA will provide adequate flow at periods of peak myocardial demand. Therefore, there is a need for a method to preoperatively assess the size and blood flow of an ITA to determine its suitability as a coronary artery bypass graft. We have found that color duplex ultrasound is a reliable noninvasive preoperative imaging modality to evaluate both right and left ITA [2]. This method can accurately define the ITA diameter, the presence of atherosclerosis, and peak systolic and end-diastolic velocities of the ITA. Figure 1 shows the typical ultrasonic appearance of a normal ITA. Based on our experience, an ITA with a diameter greater than 1.8 mm and a peak systolic velocity less than 150 cm/s is acceptable for use as a coronary artery bypass graft. We have also shown that anatomic and physiologic noninvasive ITA flow measurements are independent of age, sex, presence of diabetes, presence of hypertension, and history of previous open heart operation and do not differ between right and left ITAs in those subgroups [2, 3].

Our experience strongly supports the findings of Dignan and associates. We hope that future development of a postoperative surveillance protocol for patients who have already undergone bypass operations will provide a basis for interpreting ITA anatomy and blood flow characteristics and a conceptual frame-

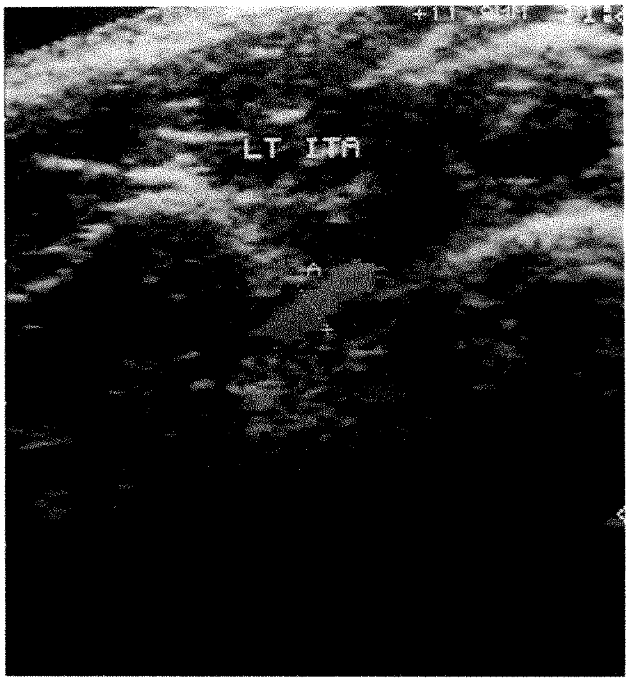


Fig 1. Typical ultrasonic appearance of a normal internal thoracic artery. (A = 3.7 mm; LT ITA = Left internal thoracic artery.)

work for understanding the prospective functional patency of this ideal conduit for myocardial revascularization.

Charles C. Canver, MD

Section of Cardiothoracic Surgery
Dartmouth Medical School
Dartmouth-Hitchcock Medical Center
One Medical Center Dr
Lebanon, NH 03756

References

1. Dignan RJ, Yeh T Jr, Dyke CM, Lutz HA III, Wechsler AS. The influence of age and sex on human internal mammary artery size and reactivity. Ann Thorac Surg 1992;53:792–7.
2. Canver CC, Ricotta JJ, Bhayana JN, Fiedler RC, Mentzer RM Jr. Use of duplex imaging to assess suitability of the internal mammary artery for coronary artery surgery. J Vasc Surg 1991;13:294–301.
3. Canver CC, Fiedler RC, Hoover EL, Ricotta JJ, Mentzer RM Jr. Noninvasive assessment of internal thoracic artery for reoperative coronary artery surgery. J Cardiovasc Surg (in press).

Reply

To the Editor:

Dr Canver's technique of evaluating mammary artery diameter, peak systolic and end-diastolic velocities, and the presence of atherosclerosis with color duplex ultrasound is very interesting and promising. I had asked Dr Dignan and his associates in the discussion of his article whether they had found any correlation of size and reactivity of the mammary artery with the presence of diabetes because of the increased incidence of atherosclerosis in diabetic patients. Dr Canver's data would suggest that the internal mammary conduit should have similar flow characteristics in diabetic patients as in the rest of the population and, therefore, the decision regarding the use of the mammary in diabetic patients should not be based on fear of inadequate flow but rather should be weighed against the possibility of mediastinal infection. This should be a useful technique for evaluating the adequacy of the mammary artery as a coronary conduit in patients when there is doubt regarding this vessel.

Frederick L. Grover, MD

Division of Cardiothoracic Surgery
University of Colorado Health Sciences Center
4200 E Ninth Ave
Denver, CO 80262

Manual Versus Stapled Bronchial Closure: Still Controversial

To the Editor:

Thirty years after the initial use of surgical staplers for bronchial closure, the development of bronchopleural fistulas after major pulmonary resection still represents one of the greatest challenges for the thoracic surgeons' current clinical practice.

Despite experimental studies by Scott and associates [1], no clear clinical advantages and no less incidence of this ominous complication are expected after mechanically stapled closure of the large bronchi. The newest report on the issue by Vester and colleagues [2] does nothing but confirm that fact. Without a clinical, prospective, randomized study comparing stapled versus sutured bronchial closure, the extended use of mechanical devices is no more than a matter of feeling, and such a feeling should not provoke a false sensation of security. Stapling is not free of likelihood of failure.

Keszler and Paris Romeu [3] reported a diminished in-hospital stay after pulmonary resection using staplers. This has important economic implications and could be a last, definitive argument for generalized bronchial stapled closure.

Rafael Aguilo, MD
Miguel Llobera, MD, PhD

Hospital "Son Dureta"
C/ Andrea Doria, 55
07014 Palma de Mallorca
Spain

References

1. Scott RN, Faraci RP, Hough A, Chretien PB. Bronchial stump closure techniques following pneumonectomy: a serial comparative study. Ann Surg 1976;184:205–11.
2. Vester SR, Faber LP, Kittle CF, Warren WH, Jensik RJ. Bronchopleural fistula after stapled closure of bronchus. Ann Thorac Surg 1991;52:1253–8.
3. Keszler P, Paris Romeu F. Stapling of the bronchus, lung and pulmonary vessels. In: Martini N, Vogt-Moykopf I, eds. Thoracic surgery: frontiers and uncommon neoplasms. St. Louis: C.V. Mosby, 1989:5–19.

Reply

To the Editor:

We are certainly pleased that Drs Aguilo and Llobera believe that we accomplished a little more than nothing, as it took considerable effort on our part to review the records and follow-up information on 2,243 patients undergoing pulmonary resection. It was not our intent to extol the virtues of bronchial stapling, nor did we reach the conclusion that it was the most effective way to close the bronchus. It was our intent to carefully review and report our incidence of fistula after stapled closure of the bronchus. We also did not advocate generalized stapling of the bronchus and did discuss the contraindications to using this technique.

In this day and age of neoadjunctive therapy for clinically advanced cancers and extrapleural pneumonectomies for tuberculosis and mesotheliomas, it would be totally inappropriate to embark on a randomized prospective study of stapled versus sutured bronchial closure. Many of these patients would have our listed contraindications for staple closure, and these include close proximity of the cancer, bronchial mucosal inflammation, and a thickened bronchus. Fifteen of the 20 pneumonectomy fistulas in our series received preoperative irradiation, and five received chemotherapy as well.

The knowledgeable thoracic surgeon makes his or her choice for bronchial closure based on reported results as well as intraoperative pathology. The decision for staple or suture closure of the bronchus is based on reported results, such as ours, coupled with good judgment.

L. Penfield Faber, MD
S. Russell Vester, MD
C. Frederick Kittle, MD
William H. Warren, MD
Robert J. Jensik, MD

Rush-Presbyterian-St. Luke's Medical Center
1753 W Congress Pkwy
Chicago, IL 60612

High-Dose Aprotinin in Emergency Coronary Artery Bypass After Thrombolysis

To the Editor:

The article by Efstratiadis and colleagues [1] illustrates the intraoperative use of high-dose aprotinin during emergency coronary artery bypass in a patient who underwent intracoronary thrombolysis with streptokinase.

Our clinical experience with aprotinin, following a randomized trial published in *The Annals* in 1989 [2], is now more than 800 patients. Aprotinin is being used as a routine in all patients undergoing cardiopulmonary bypass at our institution.

Here we report 3 cases of patients who were taken to operation soon after thrombolytic treatment. One patient was operated on immediately after intracoronary thrombolysis with urokinase (650,000 U) for evolving acute myocardial infarction, complicated by cardiac arrest with successful resuscitation in the catheterization laboratory. He had triple coronary artery bypass grafting performed.

In 2 other patients, the indication for coronary artery bypass grafting was set after thrombolysis. In 1 patient, 1.5 million units of streptokinase was infused intravenously 12 hours before operation; in the other patient, thrombolysis with recombinant tissue plasminogen activator (100 mg) was undertaken 13 hours before the operation.

All 3 patients had an uncomplicated postoperative course. Aprotinin treatment was used throughout the operation, according to the usual dosage: 2,000,000 KIU at the start of the operation, 500,000 KIU per hour, and 1,000,000 KIU added to the pump prime [2].

Intraoperative and postoperative bleeding was trivial. Total postoperative drainage was 315 mL, 550 mL, and 555 mL, respectively, in the 3 patients, and homologous transfusion was not needed. Skinner and associates [3] reported a mean postoperative blood loss of 1,450 mL in 24 patients operated on after intracoronary thrombolysis, with 5 patients bleeding in excess of 2,000 mL; average transfusion requirement of more than 8 U of blood and 8 U of plasma was reported.

The precise mechanism of action of aprotinin is still unclear. However, we believe that, although the cost of aprotinin infusion is not low, it is justified by the efficacy in reducing both bleeding and the need for transfusion, thus decreasing all related risks to the patient. We agree with Efstratiadis and colleagues, and we would like to underline their statement about the utility of aprotinin in the setting of urgent operations soon after thrombolysis, thus avoiding all problems associated with potential excessive bleeding.

Franco Alajmo, MD
Giancarlo Calamai, MD

Department of Cardiac Surgery
Policlinico di Careggi
viale Morgagni 85
50134 Florence, Italy

References

1. Efstratiadis T, Munsch C, Crossman D, Taylor K. Aprotinin used in emergency coronary operation after streptokinase treatment. Ann Thorac Surg 1991;52:1320–1.
2. Alajmo F, Calamai G, Perna AM, et al. High-dose aprotinin: hemostatic effects in open heart operations. Ann Thorac Surg 1989;48:536–9.
3. Skinner JR, Phillips SJ, Zeff RH. Immediate coronary bypass following failed streptokinase infusion in evolving myocardial infarction. J Thorac Cardiovasc Surg 1984;87:567–70.

Reply

To the Editor:

We would like to thank Drs Alajmo and Calamai for their comments on our report of the use of aprotinin (Trasylol; Bayer AG, Leverkusen, Germany) to control streptokinase-induced bleeding during emergency coronary operations [1]. We note with interest their similar findings in 3 patients as well as their policy of routine administration of aprotinin to all patients undergoing operations employing cardiopulmonary bypass.

We have continued to use aprotinin in this particular clinical setting. In a further 4 patients to that reported in our case study, we have seen a similar reduction in blood loss and need for transfusion of blood products.

As Drs Alajmo and Calamai rightly point out, the precise mode of action of aprotinin is still unclear. Although recent evidence suggests that this hemostatic effect may be implemented by preservation of platelet number and function [2], we believe that the known antiplasmin/antifibrinolytic action of aprotinin is an important part of the mechanism, and hence that it is eminently logical to administer aprotinin to patients recently given urokinase, streptokinase, or tissue-type plasminogen activator.

We see this application as yet another indication for the use of aprotinin in cardiac surgical practice. We do not currently use aprotinin for uncomplicated elective primary cardiac operations, but continue to administer it to high-risk patients, including those having reoperation, septic patients, and patients with coagulation or platelet disorders.

Theodore Efstratiadis, MD, PhD
Christopher Munsch, FRCS
David Crossman, MRCP
Kenneth M. Taylor, MD

Departments of Cardiothoracic Surgery and Cardiology
Hammersmith Hospital
Du Cane Rd
London W12 OHS
England

References

1. Efstratiadis T, Munsch C, Crossman D, Taylor K. Aprotinin used in emergency coronary operation after streptokinase treatment. Ann Thorac Surg 1991;52:1320–1.
2. Van Oeveren W, Harder MP, Roozendal KJ, Eijsman L, Wildevuur CRH. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:788–97.

Hemodynamic Effects of Pericardial Closure

To the Editor:

The article entitled "Adverse hemodynamic effects of pericardial closure soon after open heart operation" by Hunter and associates [1] is an interesting one. After reading the article one may gain the impression that closing the pericardium is not to be recommended in patients undergoing open heart operations. Our experience in the past 18 years in valvular cardiac surgery has taught us that closing the pericardium is indeed an essential prerequisite for preventing postoperative complications and catastrophic hemorrhage at a second operation. This is based on our experience, which includes valve replacement in nearly 3,000 patients and mitral valve repair in about 500 patients at our institution. This also includes 180 patients undergoing operation after previous closed mitral commissurotomy and another 160 or so patients undergoing reoperation after a previous open heart operation for valvular heart disease. It is our firm belief that closing the pericardium is based on sound surgical principle of reconstructing tissue planes and restoring functional integrity of the pericardium, in addition to avoiding risk of injury to the cardiac chambers at reoperation. The study by Hunter and associates, based on hemodynamic measurements in 10 patients, gives the erroneous impression that closing the pericardium is harmful. What is lacking in this study is the description of myocardial protection and components of the extracorporeal circuit. Although we have no firm data to substantiate our observation, we believe that both these factors are responsible for producing myocardial edema and cardiac distention. Such being the case, is it possible that myocardial protection was unsatisfactory in the group of patients studied by Hunter and associates.

Arkalgud Sampathkumar, MD

Department of Cardio Thoracic and Vascular Surgery
All India Institute of Medical Sciences
Ansarinagar, New Delhi 110029
India

Reference

1. Hunter S, Smith GH, Angelini GD. Adverse hemodynamic effects of pericardial closure soon after open heart operation. Ann Thorac Surg 1992;53:425–9.

Reply

To the Editor:

We thank Dr Sampathkumar for his comments and also reassure him that all our patients received adequate myocardial protection with cold St. Thomas's No. II crystalloid cardioplegic solution. None of the patients in the study [1] suffered intramyocardial infarction or had development of postoperative complications, and the mean hospital stay was 9 days (range, 8 to 12 days).

The stimulus for our study came from the observations in an animal model [2] in which similar hemodynamic impairment was observed on closing the pericardium, even in the absence of any cardiac procedure. These changes were completely reversed by opening the pericardium. Although we agree that there may be some degree of cardiac edema after an open heart operation, the animal study suggests that it is not a major contributing factor to the observed hemodynamic changes.

Although closing the pericardium has the theoretical advantage of protecting the heart at reoperation, in our experience of more than 150 reoperations in the last 4 years, we have encountered no major complications at resternotomy in patients in whom the pericardium was not closed.

Finally, the conclusion of our study simply points out that in critically ill patients with low cardiac output who are already requiring inotropic support, any acute embarrassment to the circulation should be avoided by leaving the pericardium open. If the surgeon decides to close the pericardium, he or she should bear in mind that measurement of systemic arterial blood pressure and other simple hemodynamic indices is insufficient to demonstrate the circulatory effects of pericardial closure. The decision of whether or not to close the pericardium should, therefore, be based on the measurement of cardiac output and systemic vascular resistance.

Steven Hunter, FRCS
Gianni D. Angelini, MD

Department of Cardiac Surgery
The University of Sheffield
Northern General Hospital
Sheffield
United Kingdom

References

1. Hunter S, Smith GH, Angelini GD. Adverse hemodynamic effects of pericardial closure soon after open heart operation. Ann Thorac Surg 1992;53:425–9.
2. Angelini GD, Fraser AG, Koning MMG, Smyllie MB, Sutherland GR, Verdouw PD. Adverse hemodynamic effects and echocardiographic consequences of pericardial closure soon after sternotomy and pericardiotomy. Circulation 1990; 82(Suppl 4):397–406.

Abrupt Cardiac Failure Using a Right VAD in the Presence of a Tricuspid Valve Prosthesis

To the Editor:

Mechanical assistance for heart failure after cardiac operations is a well-established technique. In the case of right ventricular assist devices there have been successful reports after both conventional cardiac operations and cardiac transplantation [1–6]. Patients suffering from long-standing mitral valve dysfunction with associated pulmonary vascular disease are particularly at risk of right ventricular failure after otherwise successful valve replacement or valvuloplasty. We describe a case that demonstrates the potential limitations of this technique when there is a competent prosthetic tricuspid valve.

A 59-year-old woman who had long-standing rheumatic mitral valve disease was seen with increasing dyspnea. Some 11 years earlier she had undergone mitral valve replacement with a Carpentier-Edwards porcine bioprosthesis and De Vega tricuspid annuloplasty. On examination she had signs of low cardiac output, a loud mitral systolic murmur, and pronounced tricuspid regurgitation. Transesophageal echocardiography confirmed the clinical findings of failed mitral prosthesis and severe tricuspid regurgitation. The pulmonary valve was described as competent.

At operation a calcified and dysfunctional mitral prosthesis was replaced with a size 29 Carbomedics prosthetic valve. The tricuspid valve was found to resemble a fibrous ring: there was little obvious leaflet tissue and it was believed that any attempt to make the valve competent would also render it stenotic. The valve was therefore replaced with a size 29 Carpentier bioprosthesis. After a total ischemic time of 65 minutes and closure of both atriotomies, systemic rewarming, and deairing, bypass was discontinued. Over the ensuing 20 minutes the right ventricle became increasingly distended and pulmonary artery pressure equaled that of the systemic circulation. There followed a period when right atrial pressure increased and in spite of increasing inotropic support and the administration of peripheral vasodilators there was low cardiac output. At the same time there was a decrease in left atrial pressure.

After the patient was returned to full cardiopulmonary bypass a centrifugal pump right ventricular assist device was attached. Blood was drained through a 9-mm right-angled cannula from the right atrium and returned from the Centrimed centrifugal pump through a size 24FG cannula in the proximal pulmonary artery. With a flow from the centrifugal pump of 4.5 L/min the patient was weaned from bypass with acceptable atrial and good systemic pressures. Thirty minutes later, after the administration of protamine, there was an abrupt circulatory collapse with a sudden distention of the pulmonary artery and right ventricle. A period of prolonged but unsatisfactory cardiac massage followed but both ventricles became noncontractile. At this time there was no evidence of left ventricular distention or disruption and there was no sign of thrombosis in the centrifugal pump, which continued to function whenever it was switched on. The patient died on the operating table.

Right ventricular failure after mitral valve replacement is an appropriate indication for an assist device. There was an encouraging initial response, with adequate cardiac output, although pulmonary arterial pressure maintained by the pump was at systemic level. This degree of pulmonary hypertension is often accompanied by pulmonary valve regurgitation, but any distention of the right ventricle causes tricuspid annular dilatation and off-loading into the right atrium. We hypothesize that the completely competent tricuspid valve prosthesis prevented this unloading in our patient, leading to accelerating right ventricular dilatation (as the pump continued to deliver blood under high pressure to the pulmonary artery) and then biventricular ventricular failure as the right ventricle became massively overstretched. There was no evidence of thrombosis in the pump or in the lungs. The left ventricle and mitral prosthesis were unremarkable at postmortem examination.

Our experience would suggest that a right ventricular assist device should be used with caution if there is a competent tricuspid valve prosthesis.

Steven C. Griffin, FRCS
John H. Dark, FRCS

Regional Cardiothoracic Centre
Freeman Hospital
High Heaton
Newcastle-upon-Tyne, NE7 7DN
England

References

1. Pennington DG, Merjavay JP, Swartz MT. The importance of biventricular failure in patients with postoperative cardiogenic shock. Ann Thorac Surg 1985;39:16–26.
2. Glenville BE, Ross DN. Ventricular assist devices. Br Med J 1986;292:361–2.
3. Dembitsky WP, Daily PO, Raney AA, Moores WY, Joyo CI. Temporary extracorporeal support of the right ventricle. J Thorac Cardiovasc Surg 1986;91:518–25.
4. Belcher P, Glenville BE, Cooper L. Successful use of a right ventricular assist device: case report. Br Heart J 1987;58:162–5.
5. Hooper TL, Odom NJ, Fetherston GS, Waterhouse P, Hilton CJ, Dark JH. Successful use of left ventricular assist device for primary graft failure after heart transplantation. J Heart Transplant 1988;7:385–7.
6. Odom NJ, Richens D, Glenville BE, Kirk AJB, Hilton CJ, Dark JD. Successful use of mechanical assist device for right ventricular failure after orthotopic heart transplantation. J Heart Transplant 1990;9:652–3.

CLASSIFIED ADVERTISEMENTS

Classified advertisements for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Art Carlucci, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010 (telephone: (212) 633-3806; facsimile: (212) 633-3820). All advertisements are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.50 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $18.00 per insertion for box number advertisements.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Advertisement orders should be for a maximum of 6 months; advertisements may be renewed for up to 6 months at a time. Advertisement copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery*, Desk Editorial, Classified Advertisements, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3853). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the advertisement. To respond to an anonymous advertisement, write to Box Number, *The Annals of Thoracic Surgery*, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Thoracic and cardiovascular surgeon with emphasis on pediatric/neonate cardiac surgery and cardiac transplantation is needed by a full-service thoracic and cardiovascular surgery group on the west coast. Must have ABTS certification. Excellent salary and benefits package. Please respond with curriculum vitae and case list.

Please respond to Box 702. 702K/D

Cardiovascular and thoracic surgeon to join established three-man clinic practice in Arkansas. Practice includes thoracic, cardiac, and vascular surgery. Must be board eligible and board certified in thoracic and cardiovascular surgery.

Please send CV to Donald L. Patrick, MD, 1500 Dodson Ave, Fort Smith, AR 72901; (501-782-2071). 717F/K

Cardiothoracic/vascular surgeon: board certified in general and thoracic surgery. Minimum of 2 years of practice experience. Very active private multispecialty practice. Located in western Pennsylvania. Salary leading to full partnership. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to Box 719. 719F/K

Thoracic and vascular surgeon, BE/BC, to join active (noncardiac) thoracic and vascular practice in Pittsburgh, PA. Please respond with curriculum vitae and details of experience.

Please respond to Box 720. 720F/K

Cardiothoracic surgeon, board certified/eligible, wanted to join established practice in northwest Indiana (very near Chicago). Excellent salary. Please respond with curriculum vitae.

Please respond to Box 723. 723F/K

Cardiothoracic and vascular surgeon, BE/BC, to join a well-established, very busy private practice in New England. Medical school affiliation. Excellent salary and benefits with eventual partnership.

Please respond to Box 727. 727G/L

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 728. 728G/L

Cardiothoracic surgeon, BE/BC, wanted to join established practice in mid-Michigan group of two. Ninety percent of practice is adult surgery and ten percent is general thoracic surgery. Respond with CV and names of references.

Please respond to Box 735. 735G/L

Board eligible or certified cardiovascular and thoracic surgeon needed to join a busy practice in the Southeast. Excellent salary and fringe benefits leading to partnership.

Please respond to Box 737. 737H/A

Cardiothoracic vascular surgeon, board certified or board eligible, to join well-established, busy one-man private practice in Midwest. Salary leading to partnership. Please send CV and references.

Please respond to Box 743. 743H/A

BC/BE cardiovascular and thoracic surgeon wanted to join busy two-member group in Fort Lauderdale, Florida. Recent US medical graduate preferred.

Please send CV to I. Tabry, MD, 2773 NE 37th Drive, Fort Lauderdale, FL 33308 ((305) 561-9781 after 9:00 PM). 746H/A

Cardiothoracic and vascular surgeon, board eligible or certified, to join 2-man private practice in Ft. Lauderdale, Florida.

Please send CV to Salem M. Habal, MD, 4800 NE 20th Terrace #107, Ft. Lauderdale, FL 33308; (305) 771-3220. 748H/A

Cardiothoracic surgeon, BC/BE, wanted to join adult cardiac surgery program in the South. Solo practice is very busy serving as regional referral center. First-rate medical facilities, liberal compensation package, and warm hospitality await you! Please send CV.

Please respond to Box 752. 752I/L

Cardiac surgeon wanted to join established private practice in upstate New York, primarily adult cardiac. Board certified or eligible required. New or recent graduate preferred. Please send CV and reference.

Please respond to Box 753. 753I/K

Thoracic/cardiovascular surgeon: three-man group in suburban New York doing general thoracic and peripheral vascular surgery desires new graduate of approved thoracic program with training in vascular surgery. Please respond with CV.

Please respond to Box 758. 758I/B

Cardiac, thoracic, and vascular surgeon needed for busy surgical group in Southeast. Outstanding income, benefits, working conditions, and quality of life. Excellent opportunity for recent trainee or experienced surgeon.

Please respond to Box 762. 762I/K

Cardiovascular and thoracic surgeon: BE/BC wanted to join an established, busy private practice in the Midwest. Peripheral vascular expertise desirable. Recent graduate of a university program preferred. Salary leading to full partnership. Please respond with curriculum vitae and references.

Please respond to Box 763. 763I/B

Cardiothoracic surgeon: Board certified/eligible and recently trained, to join an established and expanding private practice of cardiac surgery.

Please respond with curriculum vitae and details of experience to John M. Postel, MD, Chief of Cardiac Surgery, Cedars Medical Center, 1400 NW 12 Ave, Miami, FL 33136. 765I/K

Cardiothoracic surgeon—to join a 3-man private practice in cardiac, thoracic, and vascular surgery in the Great Lakes region. Must be board certified or eligible. Recent graduates considered. Send curriculum vitae.

Please respond to Box 766. 766I/K

BC/BE surgeon wanted to join adult cardiac and thoracic practice in Southeast. Approximately 300 cases per year. Relaxed environment. Include CV with response.

Please respond to Box 768. 768J/K

Cardiothoracic surgeon—BE/BC—to join 2-man practice in South performing adult cardiac, thoracic, and vascular surgery. Surgeon finishing training or recent graduate preferred.

Please respond to Box 770. 770J/A

Cardiothoracic and vascular surgeon to join a busy and well-established 3-man practice in mid-Michigan. Applicant should be board certified or eligible in thoracic and cardiovascular surgery. We prefer a candidate who has recently completed his or her training. Competitive salary leading to early partnership, with excellent benefits and working conditions. Please respond with CV.

Please respond to Box 772. 772J/L

Cardiothoracic surgeon, BE/BC, to join busy 3-man cardiothoracic private practice in Manchester, NH. Salary and benefits leading to partnership.

Interested applicants should send CV to Benjamin M. Westbrook, MD, 100 McGregor St, Manchester, NH 03102-3770. 775J/C

Cardiovascular and thoracic surgeon: Multispecialty group seeks second surgeon for balanced practice of adult cardiac, thoracic, and peripheral vascular surgery. Recent graduate preferred. Located on Florida's Gulf Coast, Tampa Bay area.

Please send response to H. Charles Campbell, MD, Diagnostic Clinic, 1551 West Bay Dr, Largo, FL 34640. 778J/L

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in mid-Michigan. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Please respond to Box 779. 779J/C

Cardiothoracic surgeon: BC/BE adult cardiothoracic surgeon wanted to join busy, established practice of four physicians. Physician will join large multispecialty group in metropolitan community of 130,000 in the upper Midwest. Affiliation with medical school and surgery residency available.

Please respond to Kathleen Toft, Director, Physician Recruitment, 737 Broadway, Fargo, ND 58123; or call 1-800-437-4010. 780J/L

Assistant surgeon: Cardiac, thoracic, or general surgeon with cardiac experience to join well-established 4-man group in the Midwest. Ideal for physician who desires low stress practice. Generous salary and fringe benefits. Please send curriculum vitae.

Please respond to Box 781. 781J/L

Cardiothoracic surgeon: Wanted to join a busy, well-established practice located in the Midwest. Prefer recent graduate, must be board certified or eligible, medical school affiliation possible. Respond with curriculum vitae.

Please respond to Box 782. 782J/L

Pediatric cardiothoracic surgeon: An opportunity is available at the assistant or associate professor level, depending on experience and credentials. The person in this position will be a full-time member of the faculty of the University of Tennessee, Memphis, and will carry out practice activities through the University of Tennessee Medical Group. The faculty member must be certified by the ABS and eligible for examination by the ABTS. The surgeon will work at LeBonheur Children's Medical Center, predominantly in congenital cardiac surgery, including heart and lung transplantation. Significant amounts of time will be spent in research and teaching activities, with some commitments to clinical activities in other hospitals. Experience and interest in pediatric thoracic surgery is necessary. Teaching activities involve medical students and resident surgeons. These activities include didactic lectures, formal conferences, seminars, grand rounds, assisting in the operating rooms and clinics. Research and scholarly activities are expected. The surgeon is expected to generate projects and funding.

Please respond to Donald C. Watson, MD, University of Tennessee, Memphis, 956 Court, Memphis, TN 38163. UT Memphis does not discriminate on the basis of race, sex, age, or religion and actively recruits women and minorities. The University is an EEO/affirmative action/title IX/section 504/ADA employer. 787K

Cardiothoracic surgeon needed to join established 2-man group in practice of adult cardiac, pulmonary, and vascular surgery. Must be board certified or eligible and graduate from a US medical school.

Please respond to R. W. Ruess, MD, 1834 Broadway, Cape Girardeau, MO 63701. 788K/A

Noncardiac thoracic surgeon wanted to join a group in northern New England. The practice would involve thoracic and general surgery. Must be board eligible or certified. Best in rural living. Please send CV.

Please respond to Box 791. 791K/A

Cardiothoracic and vascular surgeon urgently needed to join established practice in Midwest. Applicant must be BE/BC. Salary leading to full partnership. Please send CV and details of experience.

Please respond to Box 792. 792K/A

Thoracic and vascular surgeon, BE/BC, to join active (noncardiac) thoracic and vascular practice in central New Jersey. Please respond with curriculum vitae and details of experience. Salary leading to full partnership.

Please respond to Box 795. 795K/C

SITUATIONS WANTED

General thoracic surgeon (BC), mature, looking for community with need, preferably Northeast or Southwest and group practice. Recent 10 years general surgical experience (BC) including laparoscopy.

Please respond to Box 741. 741H/A

Cardiothoracic surgeon, 35 years old, university trained, board certified with two years busy private practice experience. Seeks opportunity with new program, individual, or group in the Southeast.

Please respond to Box 757. 757J/C

Cardiovascular surgeon—34 y/o, ABTS, AOA, university trained—one year of clinical practice. Wishes to relocate to medium size community.

Please respond to Box 760. 760I/L

American born and trained, ABTS certified, 43-y/o cardiac surgeon wishes to relocate. Extensive experience with elective and emergent cardiac surgery, thoracic and vascular surgery.

Please respond to Box 773. 773J/K

Young BC general surgeon seeking noncardiac thoracic fellowship. Need not be accredited.

Please respond to Box 785. 785K

General thoracic and general surgery combined. Board certified. Recent graduate looking for an exciting practice. Interest in endoscopic and laser surgery.

Please respond to Box 790. 790K/D

Cardiothoracic surgeon in-training in Boston until June 1993. Board eligible, young, energetic, aggressive. Interested in adult cardiac and general thoracic. Preferably group practice. Geographic location flexible.

Please call (617) 547-7313. 793K

56-y.o. Thoracic and cardiovascular surgeon, American graduate, university trained, numerous publications, advanced surgical degree. Recent 3 + 6 months tutorial in vascular and general surgery. Wishes to relocate.

Please respond to Box 794. 794K/A

Cardiovascular and thoracic surgeon, ABS certified, ABTS eligible, currently at a major university center. Excellent training in all aspects of adult cardiovascular and thoracic surgery including heart and lung transplantation. Extensive prior experience in the specialty in England. Seeks opportunity with private or academic group practice. Available July 1993. CV and references upon request.

Please respond to Box 796. 796K/A

Cardiothoracic surgeon recertified in thoracic surgery with over 5,000 open heart surgery case experience and excellent results wishes to relocate. Seeks opportunity with new program or group practice.

Please respond to Box 797. 797K

FELLOWSHIPS

Surgical residents/fellows—Clinical residency/fellowship positions available in adult and pediatric cardiothoracic surgery. Large volume of cases. New Jersey license required. Excellent salary and benefits.

Please contact Lynn B. McGrath, MD, Chairman, Department of Surgery, Deborah Heart and Lung Center, 200 Trenton Rd, Browns Mills, NJ 08015; (609) 893-6611, Ext 359. 653A/K

Fellowship in cardiovascular surgery: Fellowship available in cardiovascular surgery from July 1, 1993, to June 30, 1992, located in southern California. Suitable for individuals waiting to enter or who have completed a thoracic surgery residency. California state medical licensure a necessity.

Please send CV, references, and clinical experience to Cardiovascular Surgery Fellowship, PO Box 232348, San Diego, CA 92193. 776J/K

Fellowship in adult cardiac surgery beginning July 1993 and available for one or two years in private program performing over 600 open heart procedures yearly. Cardiac surgery training required. ECFMG and visa qualified foreign applicants accepted.

Send curriculum vitae to Donald R. Kahn, MD, 817 Princeton Ave, Suite 300, Birmingham, AL 35211. 786K/A

Postresidency clinical fellowship available in cardiopulmonary surgery with group performing over 1,200 cardiac procedures per year. Up to 25% research opportunity option available. Complete training in cardiopulmonary surgery required. US graduates must be eligible for Oregon license. FMGs must be eligible for J-1 or H-1 visa. Fellowship for one to two years beginning January 1993 or July 1993.

Please send CV and three letters of reference to Albert Starr, MD, 9155 SW Barnes Rd, Suite 240, Portland, OR 19225. 789K/L

If you are a cardiovascular and thoracic surgeon with a vascular emphasis . . .

. . . board-certified or board eligible

and looking for . . .

. . . association with a young, well-established cardiovascular and thoracic surgeon
. . . a growing practice that offers big-city medicine and a relaxed lakeside lifestyle
. . . a guaranteed income leading to full partnership
. . . privileges at a 300-bed regional medical center
. . . newly developed state-of-the-art inpatient and outpatient vascular labs
. . . a community that offers excellent schools, housing, recreational and social opportunities
. . . a location on beautiful Lake Michigan just 90 minutes from Chicago

Then we're looking for you.

Please send your curriculum vitae to Meredith Schmidt, Physician Services Representative, Mercy Memorial Medical Center, 1234 Napier, St. Joseph, MI 49085, or call (616) 927-5131.

University of California, Los Angeles
Division of Cardiothoracic Surgery

General Thoracic Surgeon

The UCLA School of Medicine, Department of Surgery is seeking applicants for a full-time Tenured Faculty position for a Board certified general thoracic surgeon who also has lung transplant experience.

In addition to proven clinical skills and research productivity, a commitment to teaching and the training of residents are important requirements.

The University of California is an equal opportunity affirmative action employer and all qualified applicants are encouraged to apply.

Please respond with curriculum vitae and references to:

Donald G. Mulder, M.D.
UCLA School of Medicine
Division of Cardiothoracic Surgery
B2-375 MDCC
10833 Le Conte Avenue
Los Angeles, California 90024

FELLOW CARDIAC SURGERY

One year fellowship available in the Section of Cardiac Surgery, Division of Thoracic Surgery, UMDNJ-Robert Wood Johnson Medical School. Rapidly expanding University Cardiac Surgery service has opportunity for Fellow to assist in operating room and help care for postoperative patients. Active research laboratories can provide opportunities for clinical and/or basic research. Situation is ideal for individual who has completed General Surgery and plans to continue into Cardiac Surgery training program. Please contact: **Alan J. Spotnitz, MD, Department of Surgery, UMDNJ-Robert Wood Johnson Medical School, One Robert Wood Johnson Place, CN 19, New Brunswick, NJ 08903-0019; Phone (908) 937-7806.** UMDNJ, NJ's university of the health sciences, is an Affirmative Action/Equal Employment Opportunity Employer, m/f/h/v, and a member of the University Health System of New Jersey.

UMD
NEW JERSEY

Cardiac Surgeon Search for:

- new programs
- additional surgeons

Knowledge of what is necessary to build and sustain a successful open heart program. Active pool of qualified candidates interested in new opportunities.

We offer fixed fees for a successful search.

dBi Healthcare, inc.
Search Consultant
100 Pine Street
Harrisburg, PA 17101
Telephone: 717/238-8855
Facsimile: 717/238-8396

Cardiothoracic Fellow

The Lankenau Hospital and Medical Research Center is a state-of-the-art medical teaching and research facility nestled in a beautiful, yet convenient suburban Philadelphia location. This past year we performed over 800 open heart surgeries including surgery for atrial and ventricular arrhythmias.

We will have a position available July 1, 1993 on our staff for a Cardiothoracic Surgical Fellow. The ideal candidate should be board eligible or certified in general surgery. Board eligible in thoracic surgery highly desired. A Pennsylvania license is a must. Clinical Fellows are welcome to apply.

Along with top of the line technology and professional colleagues, the position offers medical benefits, no city wage tax deducted and a non-smoking environment. For further information, please forward CV to: **Dr. Scott M. Goldman, Chief, Division of Thoracic & Cardiovascular Surgery, c/o Personnel Department, 100 Lancaster Avenue, west of City Line, Wynnewood, PA 19096.**

THE LANKENAU HOSPITAL MEDICAL RESEARCH CENTER

A Member of the Main Line Health Family of Hospitals.

An Equal Opportunity Employer

CARDIOTHORACIC SURGERY

The Division of Cardiothoracic Surgery at Tulane University School of Medicine is seeking applicants for a full-time academic position at the assistant/associate professor level. Applicants should be BC/BE in cardiothoracic surgery. The Division sponsors a fully approved graduate education program in cardiothoracic surgery with involvement at Tulane University Hospital, Charity Hospital and VA Medical Center.

The individual sought for this position should have an interest in academic surgery and have demonstrated expertise in research. Recommendations and correspondence should be directed to:

John D. Pigott, M.D.
Director of Cardiothoracic Surgery
Tulane University School of Medicine
1430 Tulane Avenue
New Orleans, LA 70112

EOE/AA

CARDIOTHORACIC SURGEON PROVO, UTAH

An outstanding opportunity exists in Provo, Utah, for a board certified cardiovascular surgeon. Experience is required and physician must also do peripheral vascular surgery. Call coverage is shared with two other thoracic surgeons. Excellent financial package, including relocation expenses, is available.

For more information, call or send a CV to:

IHC Physician Services
P.O. Box 57010
Murray, UT 84157-0010
1-800-888-3134

INTERMOUNTAIN HEALTH CARE

THORACOSCOPY FOR THORACIC SURGEONS

Pericardiectomy, Blebectomy, Sympathectomy, Pulmonary Resection

These two-day advanced courses consist of four hours of didactics and 11 hours of hands-on laboratory. The techniques of thoracoscopic vagotomy, wedge resection, node dissection and other advanced procedures will be taught in detail. In addition, special emphasis will be placed on developing skills in thoracoscopic suturing and stapling techniques.

COURSE DIRECTOR	COURSE MODERATOR
Karl A. Zucker, M.D.	Mark J. Krasna, M.D.

FACULTY INCLUDES
Thomas Daniels, M.D.
Richard Heitmiller, M.D.
Rodney Landreneau, M.D.
Joseph Locicero, M.D.

The faculty is skilled in the use of hand instrumentation for the advanced thoracoscopic procedures. The operating stations are directed by thoracic surgeons who bring a wealth of clinical experience to the "hands-on" classroom.

Medcom Management International, Inc.
(410) 321-5481

LOCATION
United States Endoscopy Laser Institute
Baltimore, Maryland

Courses are limited to 18 participants.

THE SOCIETY OF THORACIC SURGEONS

Surgical Video Library

-inch VHS format
ternational formats available

$25.00 each*
(includes shipping and handling)

Titles Available:

Esophageal Manometry — Indications, Technique and Computerized Assessment (Tom R. DeMeester)

En Bloc Resection of A Superior Sulcus Tumor (Robert J. Ginsberg)

Composite Valve Graft Replacement of Ascending Aorta (Cabrol Technique) and Transaortic Replacement of Mitral Valve (E. Stanley Crawford)

Graft Replacement of Thoraco-Abdominal Aortic Aneurysm (E. Stanley Crawford)

Aortic Valve Replacement with Aortic Allograft (Donald B. Doty)

Multiple Internal Mammary Artery Grafts (Alfred J. Tector)

Extended Endarterectomy for Left Anterior Descending Disease (W. Dudley Johnson)

NEW!

Sleeve Lobectomy (Douglas J. Mathisen)

Tracheal Resection (Douglas J. Mathisen)

Videos can be ordered by mail for $25.00 each* (includes shipping and handling).

Please send order along with payment to:

The Society of Thoracic Surgeons
P.O. Box 809285
Chicago, IL 60611

Allow 4-6 weeks for delivery

International formats (standard PAL and SECAM only) are available at $50.00 each, including production and shipping. **Please allow 12 weeks for delivery.**

Cardiothoracic and vascular surgeon, board certified, board eligible to join a three-man practice in the Midwest.

Salary leading to full partnership.

Please send curriculum vitae.

Please respond to:
Box 784
The Annals of Thoracic Surgery
Elsevier Science Publishing Company
655 Avenue of the Americas
New York, NY 10010

UAB
Division of Cardiothoracic Surgery

Thoracic Surgeon

University of Alabama at Birmingham

The Division of Cardiothoracic Surgery at the University of Alabama at Birmingham (UAB) seeks candidates for the Head of the Section of Non-Cardiac Thoracic Surgery.

UAB Division of Cardiothoracic Surgery has a very active clinical general thoracic surgical program and a growing lung transplant program. The successful candidate must be Board Certified in Thoracic Surgery with excellent clinical skills and strong academic interests. Position is tenure-accruing with appointment at an appropriate academic level. UAB offers an excellent compensation and benefits package.

Please respond with curriculum vitae and references to:

A. D. Pacifico, M.D.
Professor and Director
Division of Cardiothoracic Surgery
University of Alabama at Birmingham
Birmingham, AL 35294-0016

UAB IS AN EQUAL OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER
WOMEN AND MINORITIES ARE ENCOURAGED TO APPLY

Cardiovascular and thoracic surgeon: BE/BC wanted to join progressive, established cardiovascular/thoracic surgeon in a 90-doctor multispecialty group in a Big-10 University community of 100,000 with superb cultural advantages. Initial guarantee and fringes with early associateship. Subsequent income based on productivity.

For confidential consideration, please submit curriculum vitae to 663, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

S&W SCOTT & WHITE

Cardiothoracic Surgery

The Division of Cardiothoracic Surgery of Scott & White Clinic and Texas A&M University College of Medicine is seeking to fill a clinical faculty position. Applicants must be Board Certified or Board Eligible.

Scott & White is located in Temple, Texas, approximately 60 miles north of Austin and 120 miles south of Dallas/Ft. Worth. Temple is a family oriented city of 50,000 with numerous nearby lakes and outdoor activities.

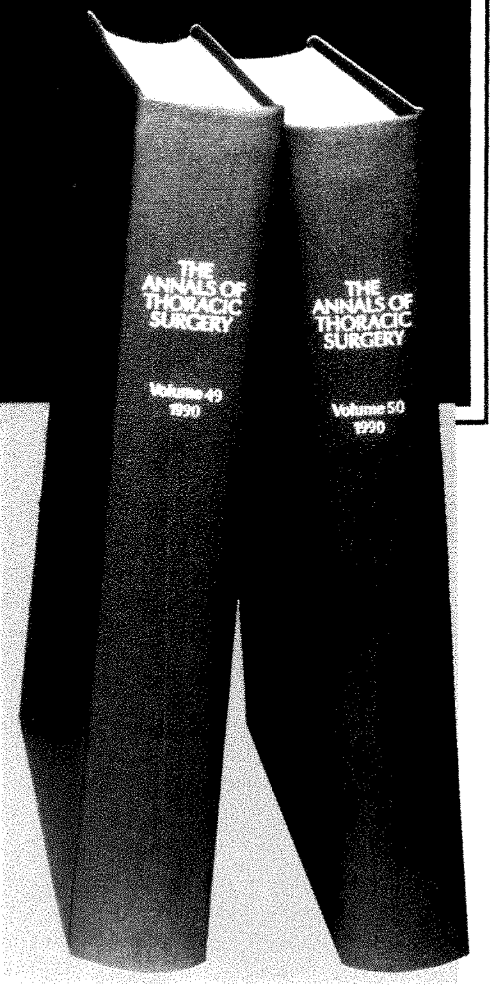
Scott & White provides an exceptionally attractive salary and benefits package to include 4 weeks vacation and 3 weeks C.M.E.

For more information, please call the Scott & White Physician Recruiting Office at 1-800-725-3627 or send a curriculum vitae to:

Michael E. Ludlow, Director
Department of Surgery
Scott & White Clinic
2401 South 31st Street
Temple, Texas 76508

An invitation for current subscribers

Bound Volumes of THE ANNALS OF THORACIC SURGERY


THE ANNALS OF THORACIC SURGERY
Volume 49
1990
THE ANNALS OF THORACIC SURGERY
Volume 50
1990

Reserve your 1991 bound volumes now! As a special service to current subscribers only, **THE ANNALS OF THORACIC SURGERY** is available in bound volumes, priced at $83.00 (US) and $100.00 (International). The two volumes for 1991 (Volumes 51 and 52) are bound in blue buckram—the same high quality binding you would find in a library—with stamped lettering on the spine. These handsomely bound volumes include:

- complete author and subject indexes
- editorial content only, with all advertising removed
- sturdy bindings for durable reference

From now on, when you receive your regular monthly copy of **THE ANNALS OF THORACIC SURGERY**, don't hesitate to tear out or mark up articles of particular interest. These specially bound volumes include every issue in perfect condition to help you keep your personal library complete, organized and current.

Reserve your 1991 bound volumes by returning the order form below.

Clip and mail to: **Elsevier Science Publishing Co., Inc.** PO Box 882, Madison Square Station, New York, NY 10159

ORDER FORM

☐ Please send me bound volumes 51 & 52 for **THE ANNALS OF THORACIC SURGERY.*** Both volumes will be shipped together for a total cost of $83.00.

☐ Please send me bound volumes 49 & 50 for **THE ANNALS OF THORACIC SURGERY** from 1990. Both volumes for $83.00.

Outside the US, please add $17.00 for postage and handling.

☐ Please start my annual standing order to receive bound volumes of **THE ANNALS OF THORACIC SURGERY.** Two bound volumes automatically will be shipped together at the end of each year.

Note: *Offer available only for subscribers to **THE ANNALS OF THORACIC SURGERY.** Please allow 3-5 weeks for receipt of your bound volumes.

Please return to:
Elsevier Science Publishing Co., Inc.
P.O. Box 882
Madison Square Station
New York, NY 10159

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC

PAYMENT

Enclosed please find my: ☐ personal check ☐ bank draft

Please charge to:

☐ Visa ☐ AMEX ☐ MasterCard (issuing bank #______)

Card #____________________ Expires__________

Signature____________________________

☐ **Please bill me.** (Postage and handling will be added to orders.)

Name____________________________

Address____________________________

City____________________________

State__________________ Zip__________

Country____________________________

Or order your bound volumes by phone

Tel. No.: ***(212) 633-3950***

Fax No.: ***(212) 633-3990***

X7AX

Cardiovascular surgeon, board eligible/certified, wanted to join an established cardiovascular program with an annual volume of 1000 open heart cases.

Located in the Northeast less than 1 hour from New York City.

Practice includes adult coronary, valve and EP surgery with some other thoracic cases.

Opportunity is available for an academic appointment at a medical school located in NYC.

Position offers excellent financial opportunity and excellent geographic location.

Send confidential reply to:

Box 798
The Annals of Thoracic Surgery
Elsevier Science Publishing Co.
655 Avenue of the Americas
New York, NY 10010

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

The Division of Cardiothoracic Surgery at The University of North Carolina Hospitals is offering a one-year position at the clinical instructor level in Thoracic Transplantation. Over the past academic year the transplant program has performed 44 thoracic transplants including heart, heart–lung, single and double lung transplants in both adults and children. This individual would be involved in selection, operative care, post-transplant care, follow-up of potential transplant patients as well as research in an active transplant laboratory. Board eligibility in Thoracic Surgery preferred. It is our belief that we can offer an excellent opportunity for individuals who have completed their thoracic surgery residency and would like a more in-depth experience in the field of thoracic transplantation. Interested applicants should write:

Benson R. Wilcox, M.D.
Professor and Chief
Division of Cardiothoracic Surgery
CB 7065 Burnett–Womack Building
Chapel Hill, NC 27599-7065
or call him directly at 919-966-3381

UNC is an Equal Opportunity, Affirmative Action Employer.

CARDIOVASCULAR HOUSE PHYSICIAN

Position available: house physician for cardiovascular surgery at the Medical Center of Delaware, Christiana Hospital.

Responsibilities: coverage of cardiovascular surgical patients and assistance to the staff cardiac surgeon during surgery.

Requirements: State of Delaware medical license or eligibility for Medical Center of Delaware institutional license, BCLS and ACLS certification, and minimal one year surgical experience are required. ICU coverage experience desirable.

Excellent salary and benefits package. Please submit curriculum vitae/résume to:

Medical Center of Delaware
Human Resource Department
Attention: Employment Director
501 W. 14th Street
Wilmington, DE 19801
FAX (302) 428-2770 EOE

ADULT CARDIOTHORACIC SURGEON

The Department of Surgery, University of California, San Francisco is seeking a cardiothoracic surgeon to be based at the San Francisco VA Medical Center. Training and experience in all aspects of adult cardiothoracic surgery required, in addition to demonstrated ability in cardiothoracic resident education, research and clinical care. Preference given to applicants having sufficient research background to apply for competitive funding. Position at assistant professor level. Send curriculum vitae to:

J. Scott Rankin, MD
Professor of Surgery and Chief
Division of Cardiothoracic Surgery
Room 593-M
University of California
San Francisco, CA 94143-0118

The University of California, San Francisco is an Equal Opportunity/Affirmative Action Employer. Women and minorities are encouraged to apply.

CARDIOVASCULAR SURGEON

Board certified/eligible cardiovascular surgeon with adult and pediatric cardiac and thoracic surgical experience. Specialized skills in arrhythmias and transplant is preferred.

The practice is a progressive, highly regarded and respected private practice located in the Midwest, in an attractive university community. Quick access to major cultural events, as well as relaxed and beautiful recreational settings.

An outstanding compensation package, including incentives, relocation and fringe benefits.

Please respond with curriculum vitae and references to:

THORACIC AND CARDIOVASCULAR INSTITUTE, P.C.
405 W. Greenlawn, Suite 220
Lansing, MI 48910
(517) 483-7579 • FAX (517) 483-7583

An Equal Opportunity Employer

RALEIGH, NORTH CAROLINA

An excellent opportunity is now available to join a two-physician Cardiovascular Surgery group in one of the most desirable regions of the country. Enjoy a busy and diverse caseload with call coverage shared equally. Minutes from the "Research Triangle," offering numerous educational and cultural opportunities. Competitive salary with partnership track. Interviewing and relocation expenses paid. Send your CV or call:

TOM HUTCHENS
JACKSON AND COKER, INC.
115 Perimeter Center Place
Suite 380 12391
Atlanta, GA 30346
1-800-544-1987

INDEX TO ADVERTISERS

Cardiothoracic Research & Education Foundation . A-19
dBi Healthcare . A-34
Intermountain Health Care . A-35
Jackson & Coker . A-40
Lankenau Hospital . A-35
Mayo Clinic . A-24
MedChem . A-14
Medcom Management International . A-35
Medical Center of Delaware . A-39
Medtronic . A-4, A-5, A-16, A-17
Mercy Memorial Medical Center . A-34
Miles . A-12
National University of Singapore . A-20
Promedica International . A-19
PSICOR . A-2
Scott & White Clinic . A-37
Sorin . Cover 2, A-1, Cover 4
St. Jude Medical . A-9, A-11
Thoracic and Cardiovascular Institute . A-40
Tulane University School of Medicine . A-35
University of Alabama at Birmingham . A-37
University of California, Los Angeles . A-34
University of California, San Francisco . A-39
University of Medicine & Dentistry of New Jersey . A-34
University of North Carolina at Chapel Hill . A-39
Vitalcor . A-22
Weisman Video Productions . A-22
W.L. Gore . A-7
Classified Advertisements . A-31 through A-33

Address advertising inquiries to Art Carlucci, Elsevier Science Publishing, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3820).

VOLUME 54 NUMBER 6 DECEMBER 1992 ISSN 0003-4975

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons
and the Southern Thoracic Surgical Association

PROGRAM FOR THE TWENTY-NINTH ANNUAL MEETING OF THE SOCIETY
OF THORACIC SURGEONS
JANUARY 25–27, 1993, SAN ANTONIO CONVENTION CENTER,
SAN ANTONIO, TEXAS, PAGE 1250

Elsevier

Volume 54 Number 6

THE ANNALS OF THORACIC SURGERY

December 1992

Contents

J. Maxwell Chamberlain Memorial Paper

Fontan Procedure for Hypoplastic Left Heart Syndrome 1025
William I. Norwood, Jr, MD, PhD, Marshall L. Jacobs, MD, and John D. Murphy, MD

Original Articles

Aprotinin Therapy for Reoperative Myocardial Revascularization: A Placebo-Controlled Study 1031
Delos M. Cosgrove III, MD, Blaine Heric, MD, Bruce W. Lytle, MD, Paul C. Taylor, MD, Roberto Novoa, MD, Leonard A. R. Golding, MD, Robert W. Stewart, MD, Patrick M. McCarthy, MD, and Floyd D. Loop, MD

Mediastinitis in Heart Transplantation 1039
Shreekanth V. Karwande, MD, Dale G. Renlund, MD, Stephanie L. Olsen, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, John A. Hawkins, MD, Roger C. Millar, MD, and John D. Marks, PE

Long-Term Effect of Total Fundoplication on the Myotomized Esophagus 1046
Philippe Topart, MD, Claude Deschamps, MD, Raymond Taillefer, MD, and André Duranceau, MD

Clinical Manifestation of Mediastinal Fibrosis and Histoplasmosis 1053
Douglas J. Mathisen, MD, and Hermes C. Grillo, MD

Postcardiotomy Centrifugal Mechanical Ventricular Support 1059
Leonard A. R. Golding, MD, Ray D. Crouch, MD, Robert W. Stewart, MD, Roberto Novoa, MD, Bruce W. Lytle, MD, Patrick M. McCarthy, MD, Paul C. Taylor, MD, Floyd D. Loop, MD, and Delos M. Cosgrove III, MD

continued on page A-6

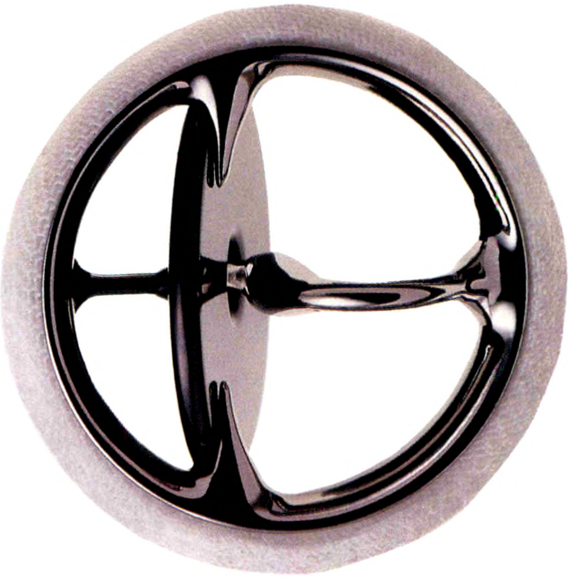
The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery*, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.

SIZES LIKE A 19

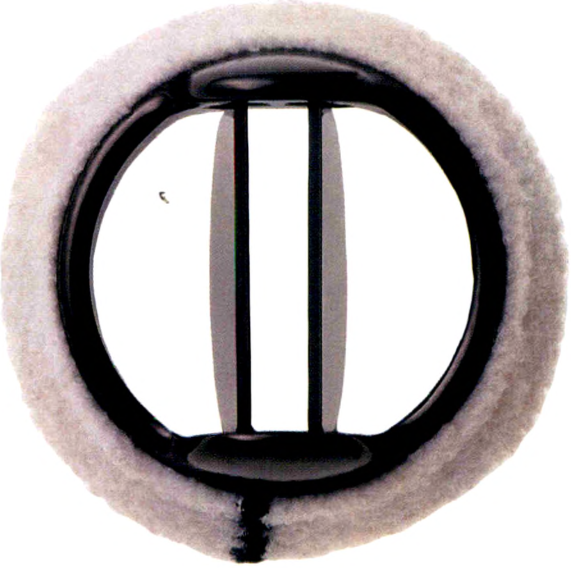
PERFORMS LIKE A 21

The 20mm Medtronic Hall™ valve is an excellent choice for the small aortic annulus. Its effective orifice area is the same as that of a Medtronic Hall 21mm valve, yet it fits the same size annulus as the St. Jude Medical 19mm bileaflet valve. The Medtronic Hall valve maximizes the flow through the small aortic annulus, significantly improving hemodynamics.

If you would like further information, please call our toll-free physician advisory number, 1-800-328-2518.
For detailed information describing intended use, warnings, precautions, and contraindications, refer to the Instructions For Use provided with the product or contact your local Medtronic representative. CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician. Valve photos were enlarged at the same percentage from actual size.



MEDTRONIC HALL™
20MM VALVE



ST. JUDE MEDICAL
19MM VALVE

	MANUFACTURER'S STATED SIZE (mm)	TISSUE ANNULUS DIAMETER[1] (mm)	INTERNAL ORIFICE AREA (cm^2)	EFFECTIVE ORIFICE AREA[2]* (cm^2)	MEAN SYSTOLIC TRANSVALVULAR GRADIENT[2]* (mmHg)
MEDTRONIC HALL™	20	20.08 ± 0.11	2.01	1.74	14.4
ST. JUDE MEDICAL	19	19.76 ± 0.40	1.63▲	1.21	28.4

[1] Data on file, Medtronic, Inc.
▲ St. Jude Medical Physician's Reference Manual.
[2] Data on file, collected by catheter pulse duplication, provided by independent consultant to Medtronic, Inc.
* At a cardiac output of 5 l/min and heart rate of 70 bpm.

MEDTRONIC HALL™
20MM VALVE

© Medtronic, Inc., 1991
All rights reserved

Medtronic

Continued from page A-3

Device-Supported Myocardial Revascularization: Safe Help for Sick Hearts 1065

Michael S. Sweeney, MD, and O. H. Frazier, MD

Early Cellular Events in the Lung Allograft 1071

Riad Adoumie, MD, Cyril Serrick, BS, Adel Giaid, PhD, and Hani Shennib, MD

Bioassay of EDRF From Internal Mammary Arteries: Implications for Early and Late Bypass Graft Patency 1078

Paul J. Pearson, MD, PhD, Paulo R. B. Evora, MD, PhD, and Hartzell V. Schaff, MD

Coronary Artery Bypass Without Cardiopulmonary Bypass 1085

Albert J. Pfister, MD, M. Salah Zaki, MD, Jorge M. Garcia, MD, Luis A. Mispireta, MD, Paul J. Corso, MD, Anjum G. Qazi, MD, Steven W. Boyce, MD, Thomas R. Coughlin, Jr, MD, and Patricia Gurny, MD

Left Atrial Isolation Associated With Mitral Valve Operations 1093

Angelo Graffigna, MD, Francesco Pagani, MD, Gaetano Minzioni, MD, Jorge Salerno, MD, and Mario Viganò, MD

Combined Carotid and Coronary Revascularization: The Preferred Approach to the Severe Vasculopath 1099

Robert J. Rizzo, MD, Anthony D. Whittemore, MD, Gregory S. Couper, MD, Magruder C. Donaldson, MD, Sary F. Aranki, MD, John J. Collins, Jr, MD, John A. Mannick, MD, and Lawrence H. Cohn, MD

Vascular Anatomy of the Gastric Tube Used for Esophageal Reconstruction 1110

Dorothea M. I. Liebermann-Meffert, MD, Renate Meier, MD, and J. Rüdiger Siewert, MD

Absent Pulmonary Valve Syndrome: Operation in Infants With Airway Obstruction 1116

Kevin G. Watterson, FRACS, Torsten K. Malm, MD, PhD, Tom R. Karl, MD, and Roger B. B. Mee, FRACS

Effect of Delay in Retroperfusion Therapy on Infarct Size Reduction 1120

Christopher M. Feindel, MD, Reena Sandhu, MSc, Jorge Cruz, MD, and Gregory J. Wilson, MSc, MD

Hyperglycemia Increases Cerebral Intracellular Acidosis During Circulatory Arrest 1126

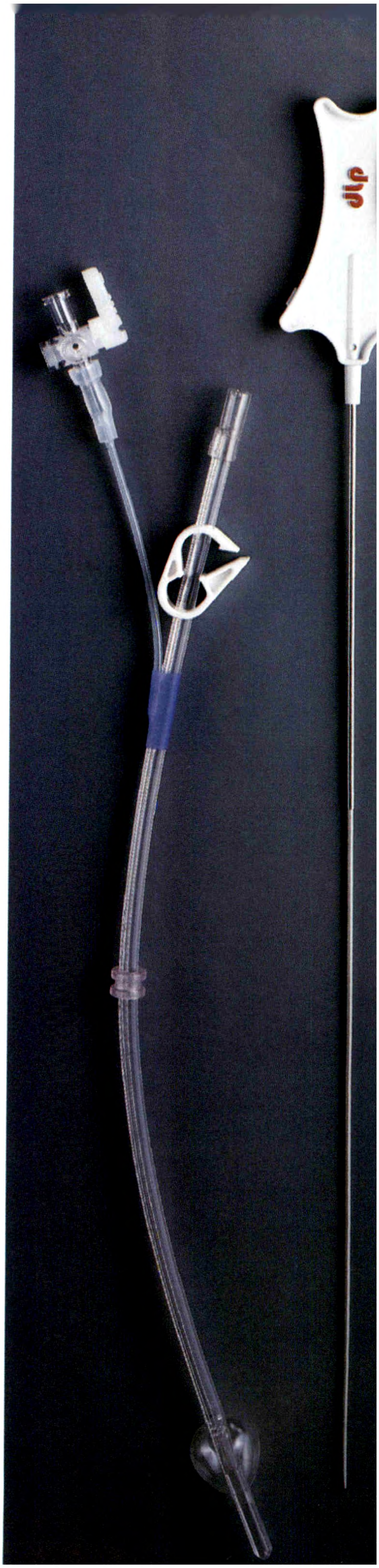
Richard V. Anderson, MD, Michael G. Siegman, MD, Robert S. Balaban, PhD, Toni L. Ceckler, PhD, and Julie A. Swain, MD

Barbiturates Impair Cerebral Metabolism During Hypothermic Circulatory Arrest 1131

Michael G. Siegman, MD, Richard V. Anderson, MD, Robert S. Balaban, PhD, Toni L. Ceckler, PhD, Richard E. Clark, MD, and Julie A. Swain, MD

continued on page A-8

DLP Introduces the New Retrograde Coronary Sinus Perfusion Cannula



DLP again extends the choice of cannula options to meet the needs of a wider range of physicians. With its 12 1/2" long body, this cannula provides the stability some physicians prefer while still resisting troublesome kinking. The Auto-Inflating RSCP cannula features a unique, bullet nose tip with three channels, for cardioplegia outflow. The channels significantly reduce jetting and additionally protect the pressure monitoring port.

THE TRU-TOUCH™ STYLET HANDLE

The RCSP cannula features DLP's newest innovation, the Tru-Touch stylet handle. Unlike other stylets that are patterned after the laparoscope, this handle gives the physician true tactile control. The Tru-Touch stylet allows the physician to use natural hand movement for fingertip controlled cannula placement.

ADDITIONAL FEATURES

- Ten, small diameter, flow-through ports reduce the possibility of inadvertent stylet caused balloon damage
- Flow-through balloon design provides better distention at lower pressures
- Integral stopcock on pressure monitoring line
- Female luer lock connector

CATALOG CODES

Auto-Inflating RCSP Cannula with Tru-Touch Handle

94835	– (Preformed Solid Stylet)	15 Fr.
94845	– (Guidewire Type Stylet)	15 Fr.

10 per carton.

The RCSP Cannula …
Another Product Innovation
from DLP!

FOR MORE INFORMATION or a product demonstration on these or any other DLP product, please contact your local DLP Surgical Sales Representative, or call DLP Toll Free: **1-800-253-1540.**

dlp

worldwide medical innovations

DLP, Inc. World Headquarters
620 Watson, SW
P.O. Box 409
Grand Rapids, MI 49501-0409
Toll-Free 1-800-253-1540
Fax 616-242-5262

DLP Medical, U.K.
Tel 44 (0) 734 731625

DLP Holland, Inc.
Tel 31 (0) 2159 37348

DLP Deutschland, Inc.
Tel 49 (0) 212 816766

Complete information on DLP cardiovascular devices including indications, contraindications and cautions, is contained in the product package labeling and should be consulted before use.

Restricted Device: Federal law (USA) restricts the sale, distribution or use of this device to, by or on the lawful order of a physician.

® DLP is a registered trademark of DLP, Inc.
™ Tru-Touch is a trademark of DLP, Inc.
TC-02696
Patent No: 5,021,045 Other Patents Pending

Continued from page A-6

Coronary Sinus Injuries During Retrograde Continuous Normothermic Blood Cardioplegia 1137

Anthony L. Panos, MD, Imtiaz S. Ali, MD, Peter L. Birnbaum, MD, Carlos A. M. Barrozo, MD, Owayed Al-Nowaiser, MD, and Tomas A. Salerno, MD

Clinical Cardiomyoplasty: Preoperative Factors Associated With Outcome 1139

Anthony P. Furnary, MD, James A. Magovern, MD, Ignacio Y. Christlieb, MD, Judith E. Orie, MD, Kathleen A. Simpson, BS, and George J. Magovern, MD

Fluosol Cardioplegia Results in Complete Functional Recovery: A Comparison With Blood Cardioplegia 1144

Jeffrey M. Pearl, MD, Hillel Laks, MD, Davis C. Drinkwater, MD, Avedis Meneshian, BS, Steven M. Martin, MD, Mark Curzan, MS, and Paul A. Chang, BS

Influence of β_1-Blockade on Myocardial Substrates Early After a Coronary Operation 1151

Örjan Wesslén, MD, Jan van der Linden, MD, Rolf Ekroth, MD, Per-Olof Joachimsson, MD, Lars Nordgren, MD, Sven-Olov Nyström, MD, Gunnar Ronquist, MD, and Hans Tydén, MD

Pleuropulmonary Aspergilloma: Clinical Spectrum and Results of Surgical Treatment 1159

Gilbert Massard, MD, Norbert Roeslin, MD, Jean-Marie Wihlm, MD, Pascal Dumont, MD, Jean-Paul Witz, MD, and Georges Morand, MD

Temporary Double Exclusion of the Perforated Esophagus Using Absorbable Staples 1165

Romeo Bardini, MD, Luigi Bonavina, MD, Maurizio Pavanello, MD, Massimo Asolati, MD, and Alberto Peracchia, MD

Vascular and Interstitial Effect of University of Wisconsin Solution on Canine Lung 1168

Helmut W. Unruh, MD

Low-Dose Aprotinin in Internal Mammary Artery Bypass Operations Contributes to Important Blood Saving 1172

Jacques P. A. M. Schönberger, MD, Peter A. M. Everts, EKP, Husam Ercan, MD, Johan J. Bredée, MD, PhD, Johan H. Bavinck, MD, Eric Berreklouw, MD, and Charles R. M. Wildevuur, MD, PhD

Safety and Efficacy of Autologous Blood Donation Before Elective Aortic Valve Operation 1177

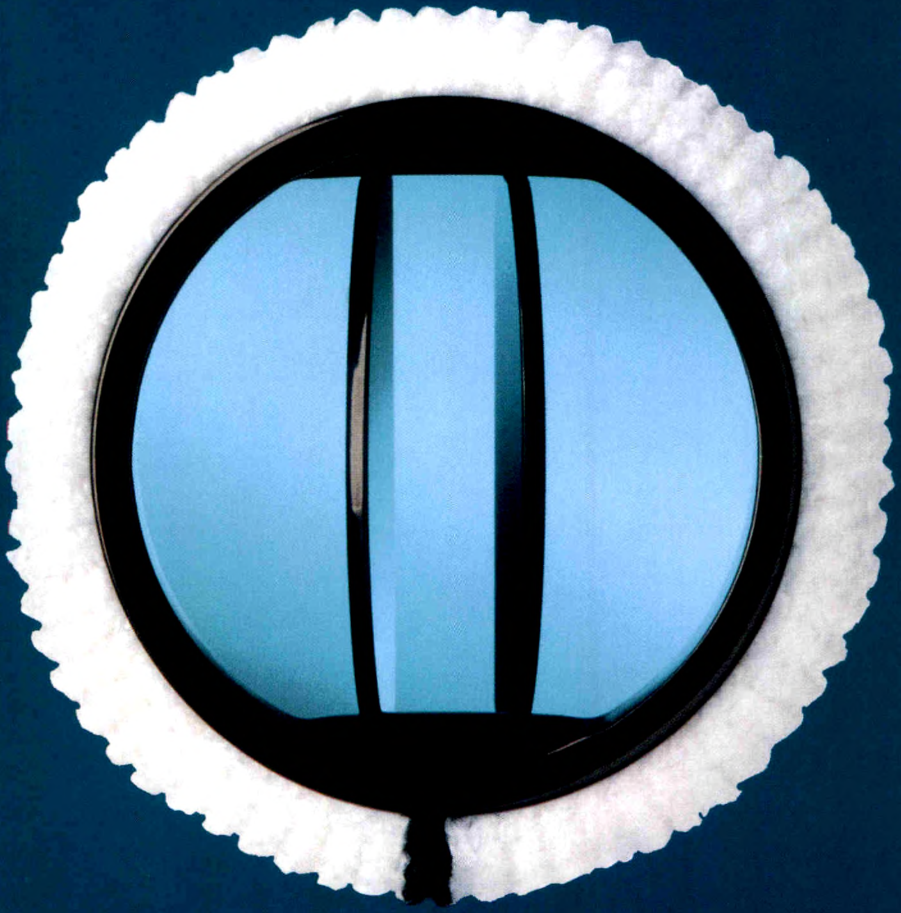
Walter H. Dzik, MD, Arlen G. Fleisher, MD, David Ciavarella, MD, Karl J. Karlson, MD, George E. Reed, MD, and Robert L. Berger, MD

Clinical and Hemodynamic Evaluation of the 19-mm Carpentier-Edwards Supraannular Aortic Valve 1182

Panny Kallis, FRCS, James F. Sneddon, MRCP, Iain A. Simpson, MRCP, Anthony Fung, FRCS, John R. Pepper, FRCS, and E. E. John Smith, FRCS

continued on page A-10

25%
more flow area



THE ST. JUDE MEDICAL® HEART VALVE
HEMODYNAMIC PLUS SERIES

Not Available in the USA

UNEQUALED PERFORMANCE
15
YEARS
SINCE 1977

ST. JUDE MEDICAL

Continued from page A-8

Optimal Approach to the Mitral Valve: Dissection of the Interatrial Groove 1186

Robert I. Larbalestier, MD, Richard B. Chard, FRCS, and Lawrence H. Cohn, MD

Pulmonary "Twinning" Procedure: Use of Lungs From One Donor for Single-Lung Transplantation in Two Recipients 1189

David A. Haydock, MD, Donald E. Low, MD, Elbert P. Trulock, MD,
Larry R. Kaiser, MD, Michael K. Pasque, MD, Ernesto Molmenti, MD, and
Joel D. Cooper, MD

Radical Laser Segmentectomy for T1 N0 Lung Cancer 1193

Ken Kodama, MD, Osamu Doi, MD, Takushi Yasuda, MD, Masahiko Higashiyama, MD, and Hideoki Yokouchi, MD

Quantitation of Particulate Microemboli During Cardiopulmonary Bypass: Experimental and Clinical Studies 1196

Jin-Feng Liu, MD, Zhao-Kang Su, MD, and Wen-Xiang Ding, MD

Case Reports

Complete Cure After a Seemingly Unsuccessful Operation for Wolff-Parkinson-White Syndrome 1203

Peter Rakovec, MD, DSc, Aleš Brecelj, MD, and Igor Zupan, MD

Pneumatocele Complicating Hyperimmunoglobulin E Syndrome (Job's Syndrome) 1206

Robert C. Shamberger, MD, Mary Ellen Wohl, MD, Antonio Perez-Atayde, MD, and
W. Hardy Hendren, MD

Surgical Treatment of Postinfarction Ventricular Septal Defect With Aortic Stenosis 1209

Lauren R. Boglioli, BS, Thomas A. Traill, MRCP, Alfred S. Casale, MD,
Bruce A. Reitz, MD, and Duke E. Cameron, MD

Pleural Liposarcoma Presenting With Respiratory Distress and Suspected Diaphragmatic Hernia 1212

Francis Carroll, MD, Marshall D. Kramer, MD, Anthony J. Acinapura, MD,
Patricia A. Tietjen, MD, Ira Wagner, MD, Stanley Oiseth, MD, and Fred Smith, MD

Retrograde Coronary Sinus Cardioplegia in the Presence of Persistent Left Superior Vena Cava 1214

David M. Shahian, MD

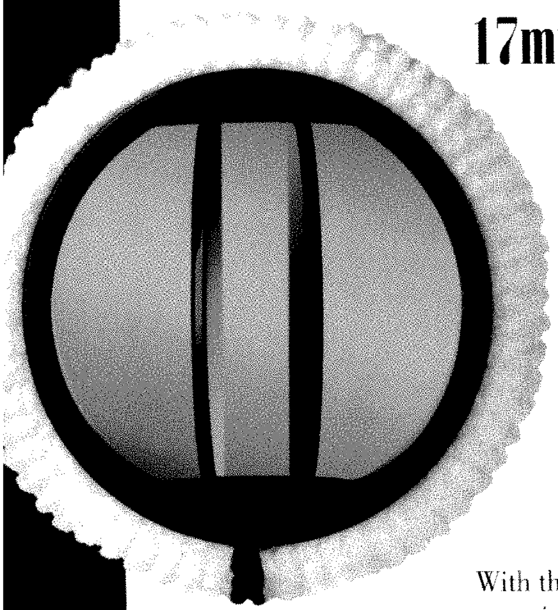
Post-Atherectomy Coronary Artery Aneurysm 1216

Amram J. Cohen, MD, Alan Banks, MD, Patrick Cambier, MD, and Fred H. Edwards, MD

continued on page A-14

The Hemodynamic Plus Series

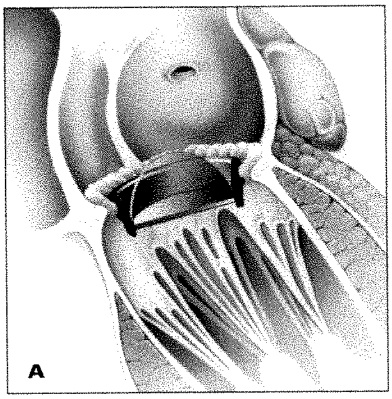
25% more flow area for patients with a 17mm to 21mm annulus



ST. JUDE MEDICAL®
HEART VALVE
HEMODYNAMIC
PLUS SERIES

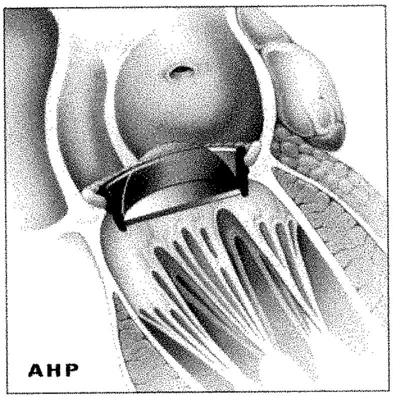
- ***Proven St. Jude Medical® heart valve design and quality***
- ***Larger orifice area***
- ***Smooth laminar flow for enhanced thromboresistance***
- ***Improved implant position***

With the Hemodynamic Plus (HP) Series valves we took sewing cuff material out of the annulus and added more orifice area.



A

Standard St. Jude Medical® aortic valve implant position



AHP

HP Series valve implant position

The HP Series valves offer you improved hemodynamics for patients with a 17mm to 21mm annulus. For 15 years surgeons and over 450,000 patients have relied on us for the best. Contact your St. Jude Medical, Inc. representative and we'll show you how the best just got better.

Not available in the USA

UNEQUALED PERFORMANCE
15
YEARS
SINCE 1977

ST. JUDE MEDICAL

Corporate Headquarters
St. Jude Medical, Inc.
One Lillehei Plaza
St. Paul, Minnesota 55117 USA

Customer Service
(612) 483-2000

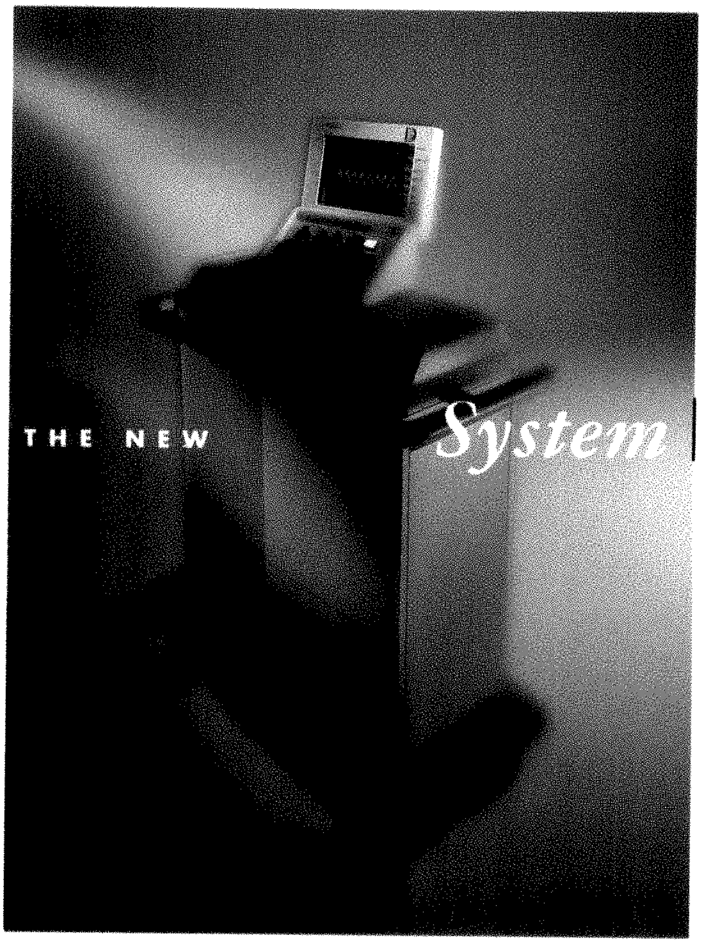
24-hour Technical/ Professional Consultation
Telephone (800) 328-9634 (USA)
(612) 483-2000
Fax (612) 482-8318

European Headquarters
St. Jude Medical Europe, Inc.
Belgian Branch
Excelsiorlaan 79
1930 Zaventem, Belgium

Customer Service
Telephone 32-2-719-68-11
Telex 20857SJMEUR
Fax 32-2-725-51-62

St. Jude Medical is a registered trademark of St. Jude Medical, Inc.
Refer to the physician's manual provided with each device for detailed instructions for use, warnings, precautions and possible adverse device effects. CAUTION: FEDERAL LAW (USA) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.
Copyright 1992 St. Jude Medical, Inc. All rights reserved. Printed in the USA. WW099220040EN

Datascope *believes that good partners listen to one another. The best ones think al*



INTRODUCING THE NEW *System* **95**

Intra-aortic balloon pum

you – anticipating your needs and responding dependably and intelligently.

For twenty years, we've been listening to the needs of cardiac specialists. Everything we've heard has resulted in the new System 95, an intra-aortic balloon pump so advanced that it almost speaks for itself.

With broader triggering options to cover more situations. Timing functions that self adjust even to complex cardiac rhythms. A variety of help screens and alarms to deal with virtually every situation. All controls, including manual override, easily accessible from the front of the machine. And with smart, simple features like a 270° rotating monitor and a permanently attached doppler.

The System 95 represents our latest advance in IABP technology, the latest partner in a series of equipment, tools and technology designed to support cardiac specialists and their patients by listening well and responding – just like Datascope.

MAN + MACHINE. *Brilliant Partners.*

1-800-288-2121

Datascope®

Continued from page A-10

Giant Intrapericardial Solitary Fibrous Tumor 1219

Uberto Bortolotti, MD, Francesco Calabrò, MD, Monica Loy, MD, Giuseppe Fasoli, MD, Giuseppe Altavilla, MD, and Domenico Marchese, MD

Management of Severe Bronchial Ischemia After Bilateral Sequential Lung Transplantation 1221

Derya Oturanlar, MD, Walter Klepetko, MD, Michael Grimm, MD, Adelheid End, MD, Wilfried Wisser, MD, Thomas Wekerle, MD, and Ernst Wolner, MD

How to Do It

Permanent Pacemaker Implantation in Premature Infants Less Than 2,000 Grams of Body Weight 1223

Mikio Ohmi, MD, Motohisa Tofukuji, MD, Kaori Sato, MD, Takahiko Nakame, MD, Naoshi Sato, MD, Kiyoshi Haneda, MD, and Hitoshi Mohri, MD

Replacement of Paracorporeal Ventricular Assist Devices 1226

Douglas P. Lohmann, ME, Lawrence R. McBride, MD, D. Glenn Pennington, MD, and Marc T. Swartz, BA

Inverted Y Incision for Accurate Tailoring of Patches and Vessels 1228

Darryl M. Hoffman, FRCS, and Robert W. M. Frater, FRCS

Repairing the Degenerative Anterior Mitral Leaflet 1229

John M. Alvarez, FRACS, Narcissus Teoh, MB, BS, and Cedric W. Deal, FRACS

Classics in Thoracic Surgery

The Nissen Fundoplication 1231

F. Henry Ellis, Jr, MD, PhD

Current Review

Release of Vasoactive Substances During Cardiopulmonary Bypass 1236

Stephen W. Downing, MD, and L. Henry Edmunds, Jr, MD

Correspondence

Team Approach for Clinical Cardiac Surgery Research 1244

Charles C. Canver, MD, and Roger C. Fiedler, PhD

Length of the In Situ Right Gastroepiploic Artery for Coronary Artery Bypass 1244

Giuseppe Tavilla, MD

continued on page A-18

Announcing research opportunities in blood conservation

Two $25,000 grants supported by Miles Inc.

1. Clinical research in blood conservation in thoracic surgery:	$25,000
2. Clinical research in blood conservation in cardiovascular anesthesia:	$25,000

Grant Information

☐ Both grants are provided by Miles Inc., Pharmaceutical Division; selection is by an independent, highly-qualified selection committee

☐ Eligibility is limited to physicians who have been in academic staff positions for no more than four years

☐ No more than 25% of the grant is to be used by the physicians' institution for indirect costs

☐ Clinical research resulting from the grant will be submitted for publication by the physician

Grant deadline:
March 15, 1993

Grant Announcement by
May 15, 1993

To request application:
Call Bruce Leeb & Company
(201) 612-8919

MILES
Pharmaceutical
Division

Printed in USA 1992

Grant Selection

☐ The grant selection committee is chaired by

Michael N. D'Ambra, M.D.
Director, Cardiac Anesthesia Group
Massachusetts General Hospital
Boston, Massachusetts

☐ Dr. D'Ambra is joined in the selection of the grantees by

Leonard L. Firestone, M.D.
Chief of Cardiac Anesthesia
University of Pittsburgh
Pittsburgh, Pennsylvania

Christina T. Mora, M.D.
Assistant Professor of Anesthesiology
Emory University School of Medicine
Atlanta, Georgia

Hartzell V. Schaff, M.D.
Consultant, Cardiovascular Surgery
Professor of Surgery
Mayo Clinic
Rochester, Minnesota

Craig R. Smith, M.D.
Director of Cardiopulmonary Transplant Program
Columbia Presbyterian Medical Center
Associate Professor Clinical Surgery, College of Physicians and Surgeons of Columbia University
New York, New York

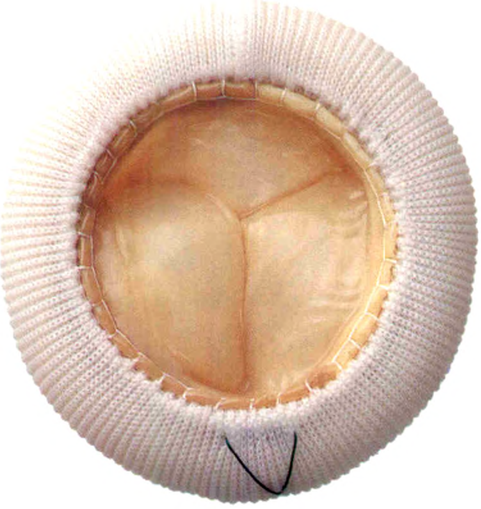
Peter K. Smith, M.D.
Assistant Professor of Surgery
Assistant Professor of Biomedical Engineering
Duke University Medical Center
Durham, North Carolina

EXPERIENCE

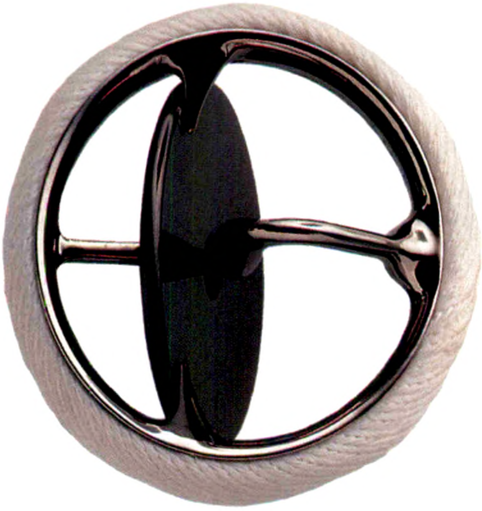
THAT

ADDS

UP



+



Medtronic Hancock® Valve
Celebrating Over 20 Years

Medtronic Hall™ Valve
Celebrating 15 Years

If you would like further information, please call our toll-free physician advisory number, 1-800-328-2518. For detailed information describing intended use, warnings, precautions, and contraindications, refer to the Instructions For Use provided with the product or contact your local Medtronic representative. CAUTION: Federal law (U.S.A.) restricts this device to sale by or on the order of a physician.

[1] Data on file, Medtronic, Inc.

= 35

Years of Combined Experience

For over 20 years, our Medtronic Hancock® tissue valve has established a history of solid clinical experience. A history longer than any other commercially available porcine bioprosthesis.

For 15 years the Medtronic Hall™ mechanical valve has had unsurpassed durability. Its hemodynamic performance rivals that of any mechanical valve – with superior performance in the small aortic annulus.[1]

Add our experience to yours.

UC9202206EN
© Medtronic, Inc. 1992
All Rights Reserved

Medtronic

Continued from page A-14

Reply
Hisayoshi Suma, MD

Electrical Instability During Reperfusion 1245
William L. Holman, MD

Pulmonary Pseudotumor 1246
Hussam A. Fadhli, MD

Hemolysis After Open Heart Operations 1246
Alessandro Golino, MD, Paolo Stassano, MD, and Nicola Spampinato, MD
Reply
Yutaka Okita, MD, and Shigehito Miki, MD

Penetrating Cardiac Trauma 1247
Rao R. Ivatury, MD, and Michael Rohman, MD
Reply
Christopher J. Knott-Craig, MD

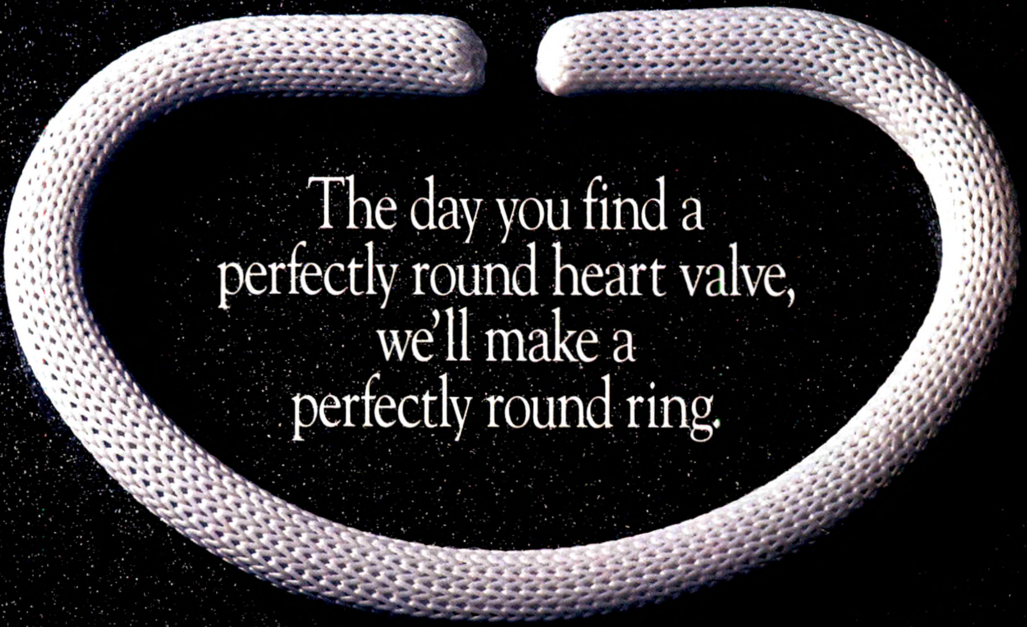
Surgery of Aortic Dissections With GRF Glue 1248
Harald E. Zeplin, MD

Modified Retractor to Prevent Peripheral Nerve Injury 1249
Nelson Ancalmo, MD

Announcements

Information for Authors A-31, 32
Guidelines for the Submission of Electronic Manuscripts A-33
Events of Interest A-34, 35
Forthcoming Articles A-37
Notice From The Society of Thoracic Surgeons 1181
Notice From the American Board of Thoracic Surgery 1205, 1215
The Society of Thoracic Surgeons: Twenty-ninth Annual Meeting 1250
Twenty-sixth Postgraduate Program, The Society of Thoracic Surgeons 1251
Program for the Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons 1252
Classified Advertisements A-39, 40, 41
Index to Advertisers A-42

continued on page A-20



Carpentier-Edwards® Annuloplasty Rings.
The only rings designed for remodeling annuloplasty.

Edwards CVS Division

© Copyright 1990. Baxter Healthcare Corporation. All rights reserved.

Baxter

Continued from page A-18

Index to Volume 54

Author Index 1265

Subject Index 1285

GENERAL INFORMATION *The Annals of Thoracic Surgery* is indexed/abstracted in *Index Medicus, Current Contents/Clinical Practice/Life Sciences, Excerpta Medica, Reference Update,* and *Biological Abstracts.*

Please direct orders for subscriptions, single copies, and back issues; changes of address; and claims for missing issues to: Journals Fulfillment Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Claims for missing issues can be honored only up to 3 months for domestic addresses, 6 months for foreign addresses. Duplicate copies will not be sent to replace ones undelivered through failure to notify Elsevier of change of address.

The Annals of Thoracic Surgery (ISSN 0003-4975) is issued monthly in two indexed volumes per year by Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. Printed in USA at 2901 Byrdhill Road, Richmond, VA 23228. Subscription prices per year: Institution: $165.00; individual, $95.00; interns and residents, $57.50. Outside USA, add $35.00 for surface postage and handling. For air delivery to USA, Canada, and Mexico, add $80.00; to Europe, $70.00 (via surface airlift); to Japan, $85.00; and to the rest of world, $160.00. Second class postage paid at New York, NY, and at additional mailing offices. Postmaster: Send address changes to *The Annals of Thoracic Surgery*, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone (212) 989-5800.

Microfilm copies are available through University Microfilms International, 300 North Zeeb Road, Ann Arbor, MI 48106.

Reprints, except special orders of 100 or more, are available from the authors.

Advertising inquiries should be addressed to: Art Carlucci, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3880).

The publisher assumes no responsibility for any injury and/or damage to persons or property as a matter of products liability, negligence, or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. No suggested test or procedure should be carried out unless, in the reader's judgment, its risk is justified. Because of rapid advances in the medical sciences, we recommend that the independent verification of diagnoses and drug dosages should be made. Discussions, views, and recommendations as to medical procedures, choice of drugs, and drug dosages are the responsibility of the authors.

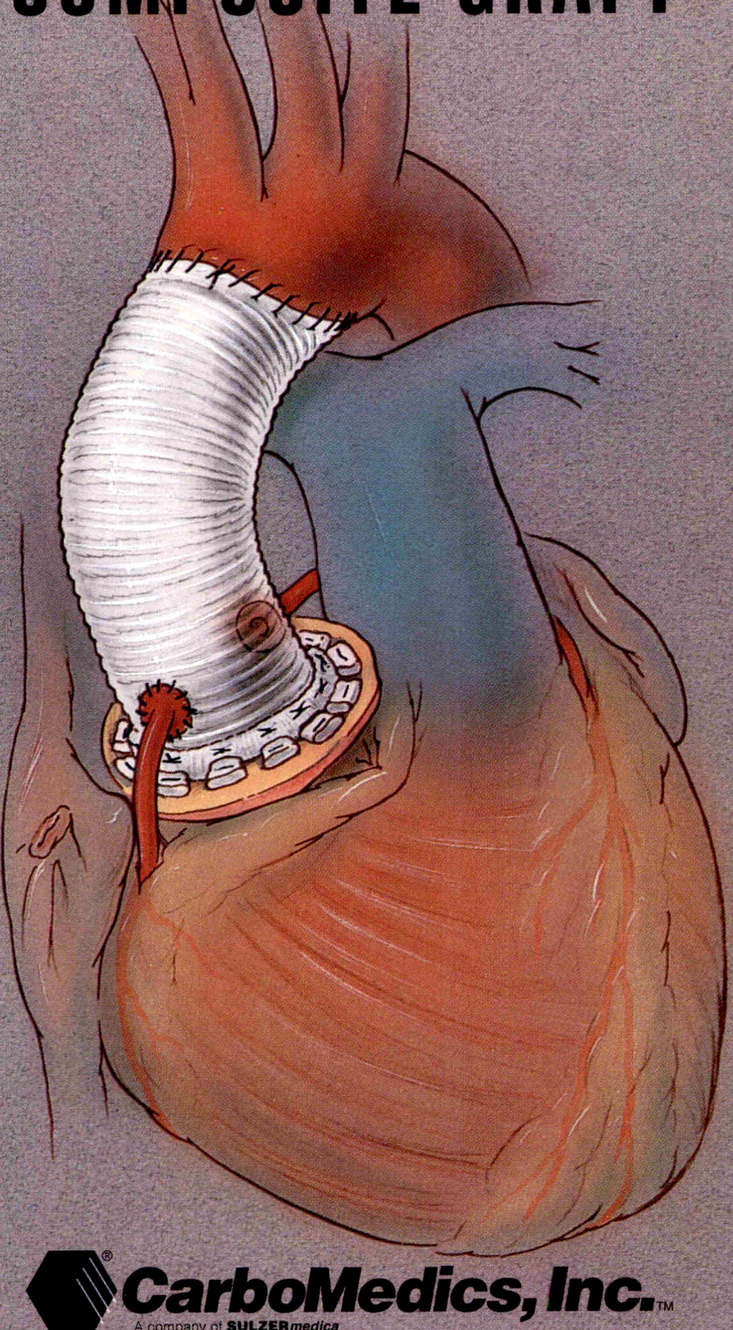
Although all advertising material is expected to conform to ethical (medical) standards, inclusion in this publication does not constitute a guarantee or endorsement of the quality or value of such product or of the claim made of it by its manufacturer.

This journal has been registered with the Copyright Clearance Center, Inc. Consent is given for the copying of articles for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition that the copier pay through the Center the per copy fee stated in the code on the first page of each article for copying beyond that permitted by the US Copyright Law. The appropriate fee should be forwarded with a copy of the first page of the article to the Copyright Clearance Center, Inc, 27 Congress Street, Salem, MA 01970. If no code appears on an article, the author has not given broad consent to copy, and permission to copy must be obtained directly from the author. This consent does not extend to other kinds of copying, such as for general distribution, resale, advertising and promotional purposes, or for creating new collective works. All inquiries regarding copyrighted material from this publication, other than reproduction through the Copyright Clearance Center, should be directed to Rights and Permissions Department, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010; (212) 633-3977.

This journal is printed on acid-free paper.

© 1992 by The Society of Thoracic Surgeons

CARBO-SEAL™
THE FIRST
ZERO POROSITY
COMPOSITE GRAFT



CarboMedics, Inc.™
A company of **SULZER***medica*

THE HEART VALVE COMPANY

1300 East Anderson Lane
Austin, Texas, USA 78752
(512) 873-3200 Facsimile (512) 873-3350

This product is not available in the United States.

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Editor

Thomas B. Ferguson, MD, St. Louis, MO

Herbert Sloan, MD, Editor 1969–1984
John D. Steele, MD, Editor 1964–1969

Associate Editors

John R. Benfield, MD, Sacramento, CA

Anthony R. C. Dobell, MD, Montreal, Canada

Marvin M. Kirsh, MD, Ann Arbor, MI

Hassan Najafi, MD, Chicago, IL

J. Kent Trinkle, MD, Book Review Editor
University of Texas Health Science Center
7703 Floyd Curl Drive, San Antonio, TX 78284-7841

Editorial Board

Hendrick B. Barner, MD, New Hyde Park, NY
Harvey W. Bender, Jr, MD, Nashville, TN
Ray Chu-Jeng Chiu, MD, PhD, Montreal, Canada
Lawrence H. Cohn, MD, Boston, MA
Jack G. Copeland III, MD, Tucson, AZ
Delos M. Cosgrove III, MD, Cleveland, OH
Timothy J. Gardner, MD, Baltimore, MD
William A. Gay, Jr, MD, Salt Lake City, UT
Robert A. Guyton, MD, Atlanta, GA
Clement A. Hiebert, MD, Windham, ME
Takashi Iwa, MD, Kanazawa, Japan
Robert B. Karp, MD, Chicago, IL
James E. Lowe, MD, Durham, NC
Douglas J. Mathisen, MD, Boston, MA
Philippe Menasché, MD, PhD, Paris, France
William I. Norwood, Jr, MD, Philadelphia, PA
John L. Ochsner, MD, New Orleans, LA
Mark B. Orringer, MD, Ann Arbor, MI
Peter C. Pairolero, MD, Rochester, MN
Richard M. Peters, MD, Palo Alto, CA
W. Gerald Rainer, MD, Denver, CO
Charles L. Roper, MD, St. Louis, MO
Thomas W. Shields, MD, Chicago, IL
Jaroslav Stark, MD, London, England
Larry W. Stephenson, MD, Detroit, MI
Kenneth M. Taylor, MD, London, England

Administrative Editor

Carol L. Blasberg, St. Louis, MO

Editorial Office

The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

To provide a place for ALL thoracic surgeons to relate experiences which will help other practicing thoracic surgeons give better patient care.
Herbert Sloan, MD

"He's still bleeding -- is it heparin?"

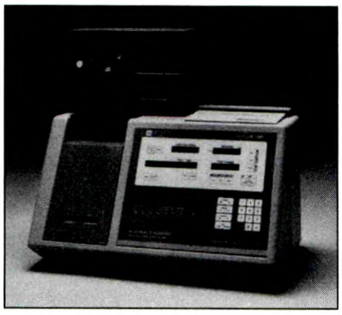
Get the answers from Medtronic HemoTec.

The benefits of heparin are undeniable. For modern surgical procedures, it has become as indispensable as a scalpel. However, heparin can complicate the process of identifying the causes of post-op bleeding.

Medtronic HemoTec gives you the tools to isolate heparin and other causes of bleeding, whether chemical, physiological or mechanical. This allows you to intervene sooner on your patients' behalf, at less cost, and lessens the need for blood products.

Our Automated Coagulation Timer and Heparinase cartridge provide activated clotting time tests that screen for heparin. This accurate, cost-effective way to get "Yes" or "No" answers quickly is available only from Medtronic.

The Hepcon/HMS® delivers quantitative data on heparin dose response, heparin concentration, and protamine reversal dosage. This fully automated system aids in differential diagnosis, identification of coagulopathies and other causes of bleeding. Our products come with a full line of Quality Controls, and our Hemostasis Specialists are experts on CLIA compliance.



Let Medtronic HemoTec answer your questions about hemostasis management. Call or write: Medtronic HemoTec, 7103 South Revere Parkway, Englewood, CO 80112-3992; phone **1-800-525-7007**.

Medtronic

HemoTec - The authority in Hemostasis Management

© 1992 Medtronic Hemotec, Inc.

The Society of Thoracic Surgeons

Officers

President	Vincent L. Gott, MD
Vice President	Denton A. Cooley, MD
Secretary	Richard P. Anderson, MD
Treasurer	Nicholas T. Kouchoukos, MD
Editor	Thomas B. Ferguson, MD
Historian	W. Gerald Rainer, MD

Councillors at Large

Leonard L. Bailey, MD
James L. Cox, MD
H. Storm Floten, MD
Timothy J. Gardner, MD
Robert J. Ginsberg, MD
Peter C. Pairolero, MD

Business Manager
Walter G. Purcell

Southern Thoracic Surgical Association

Officers

President	William A. Cook, MD
President-Elect	Gordon F. Murray, MD
Vice President	Joseph I. Miller, Jr, MD
Secretary-Treasurer	Hendrick B. Barner, MD
Editor	Thomas B. Ferguson, MD
Historian	Hawley H. Seiler, MD

Council

Robert M. Sade, MD
Chairman
William C. Alford, Jr, MD
Hendrick B. Barner, MD
William A. Cook, MD
Timothy J. Gardner, MD
Joseph I. Miller, Jr, MD
Gordon F. Murray, MD
D. Glenn Pennington, MD
William F. Sasser, MD
Thomas B. Ferguson, MD (Ex Officio)

Business Manager
Walter G. Purcell

For information about either organization, contact either The Society of Thoracic Surgeons or the Southern Thoracic Surgical Association at 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610 (facsimile: (312) 527-6635).

THE FIRST
INTERNATIONAL SYMPOSIUM OF

THORACOSCOPIC SURGERY

JANUARY 22-23, 1993 • SAN ANTONIO, TEXAS

PROGRAM DIRECTOR

Michael Mack, M.D.
Humana Hospital-
Medical City Dallas

IMMEDIATELY PRIOR TO STS

. . . .

THE FIRST INTERNATIONAL SYMPOSIUM OF THORACOSCOPIC SURGERY

JANUARY 22-23, 1993

PLEASE PRINT OR TYPE

Send Information

Register Me

Name: First	Last	M.D., Prof., R.N.	Companion
Mailing Address		Hospital	
City	State	Zip	Country
Telephone	Fax	Specialty	

Mail to: PROMEDICA INTERNATIONAL • 620 Newport Center Drive, Suite 575 • Newport Beach, CA 92660 • USA
Contact: Margo Irr • TEL (714) 640-5870 Ext 28 • FAX (714) 759-6911

Cardiovascular and thoracic surgeon: BE/BC wanted to join progressive, established cardiovascular/thoracic surgeon in a 90-doctor multispecialty group in a Big-10 University community of 100,000 with superb cultural advantages. Initial guarantee and fringes with early associateship. Subsequent income based on productivity.

For confidential consideration, please submit curriculum vitae to 663, The Annals of Thoracic Surgery, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

CARDIOTHORACIC SURGEON PROVO, UTAH

An outstanding opportunity exists in Provo, Utah, for a board certified cardiovascular surgeon. Experience is required and physician must also do peripheral vascular surgery. Call coverage is shared with two other thoracic surgeons. Excellent financial package, including relocation expenses, is available.

For more information, call or send a CV to:

IHC Physician Services
P.O. Box 57010
Murray, UT 84157-0010
1-800-888-3134

INTERMOUNTAIN HEALTH CARE

Cardiothoracic and vascular surgeon, board certified, board eligible to join a three-man practice in the Midwest.

Salary leading to full partnership.

Please send curriculum vitae.

Please respond to:
Box 784
The Annals of Thoracic Surgery
Elsevier Science Publishing Company
655 Avenue of the Americas
New York, NY 10010

Cardiothoracic Fellow

The Lankenau Hospital and Medical Research Center is a state-of-the-art medical teaching and research facility nestled in a beautiful, yet convenient suburban Philadelphia location. This past year we performed over 800 open heart surgeries including surgery for atrial and ventricular arrhythmias.

We will have a position available July 1, 1993 on our staff for a Cardiothoracic Surgical Fellow. The ideal candidate should be board eligible or certified in general surgery. Board eligible in thoracic surgery highly desired. A Pennsylvania license is a must. Clinical Fellows are welcome to apply.

Along with top of the line technology and professional colleagues, the position offers medical benefits, no city wage tax deducted and a non-smoking environment. For further information, please forward CV to: **Dr. Scott M. Goldman, Chief, Division of Thoracic & Cardiovascular Surgery, c/o Personnel Department, 100 Lancaster Avenue, west of City Line, Wynnewood, PA 19096.**

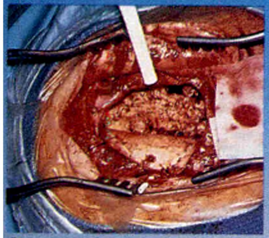
THE LANKENAU HOSPITAL MEDICAL RESEARCH CENTER

A Member of the Main Line Health Family of Hospitals.

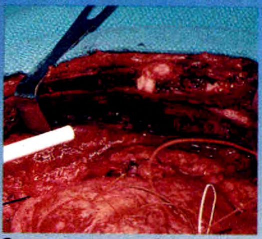
An Equal Opportunity Employer

HEMOSTASIS.

The easy way, any way, every way, the versatile spray.

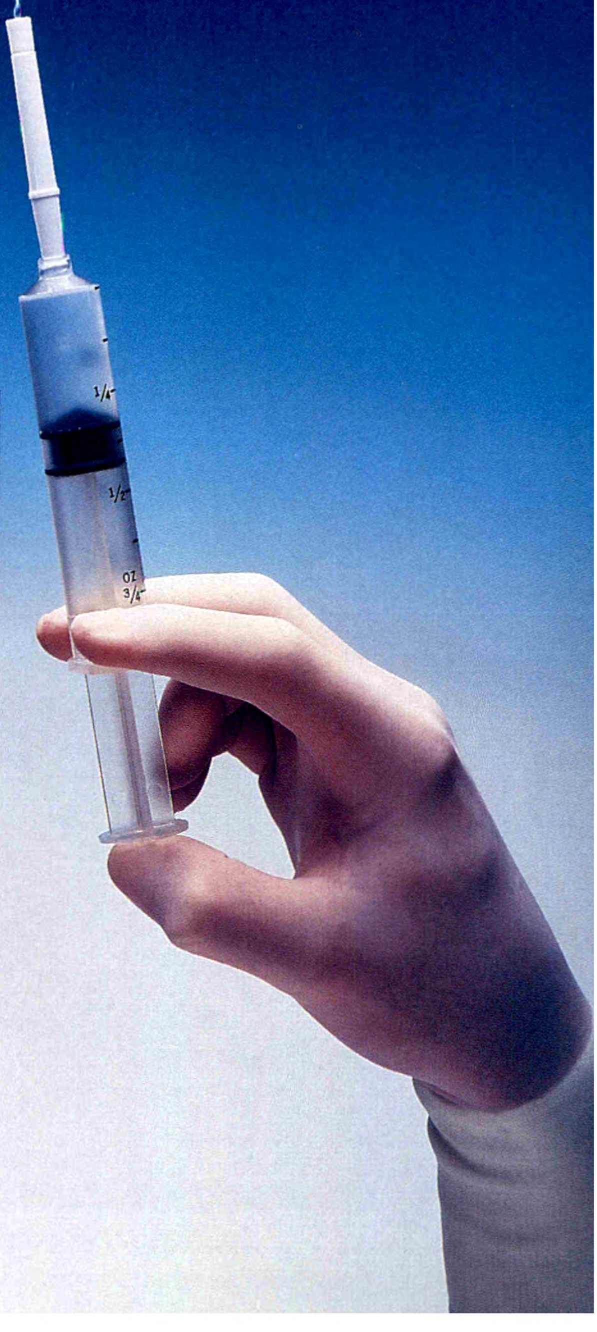


Accesses hard-to-reach sites
In *neurosurgery*, THROMBOGEN Thrombin provides hemostasis in hard-to-reach sites, such as deep tumor beds.



Sprays at any angle
In *cardiovascular surgery*, control oozing under the sternum by spraying THROMBOGEN Thrombin upside down.

Covers broad areas evenly
In *burn surgery*, an even and consistent spray of THROMBOGEN Thrombin controls bleeding of broad areas, such as donor sites.



THROMBOGEN*
Topical Thrombin, USP

Johnson & Johnson
MEDICAL INC.

*TRADEMARK © JJM, INC. 1991

For further product information, call 1-800-433-5009.

Please see following page for brief summary of Prescribing Information.

Thrombin, Topical USP THROMBOGEN*
(Bovine origin)

Before prescribing please see full prescribing information. A Brief Summary follows: Thrombin, Topical USP THROMBOGEN* must not be injected! Apply on the surface of bleeding tissue as a solution or powder

INDICATIONS AND USAGE: THROMBOGEN Thrombin is indicated as an aid in hemostasis wherever oozing blood from capillaries and small venules is accessible.

In various types of surgery, solutions of THROMBOGEN Thrombin may be used in conjunction with Absorbable Gelatin Sponge, USP for hemostasis.

CONTRAINDICATIONS: THROMBOGEN Thrombin is contraindicated in persons known to be sensitive to any of its components and/or to material of bovine origin.

WARNING: Because of its action in the clotting mechanism, THROMBOGEN Thrombin must not be injected or otherwise allowed to enter large blood vessels. Extensive intravascular clotting and even death may result. THROMBOGEN Thrombin is an antigenic substance and has caused sensitivity and allergic reactions when injected into animals.

PRECAUTIONS: General: Consult the Absorbable Gelatin Sponge, USP product labelling for complete information for use prior to utilizing the thrombin-saturated-sponge procedure.

Pregnancy-Teratogenic effects: Pregnancy Category C. Animal reproduction studies have not been conducted with Thrombin, Topical USP (Bovine origin). It is also not known whether Thrombin, Topical USP (Bovine origin) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thrombin, Topical USP (Bovine origin) should be given to a pregnant woman only if clearly indicated.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Allergic reactions may be encountered in persons known to be sensitive to bovine materials.

DOSAGE AND ADMINISTRATION: General: Solutions of THROMBOGEN Thrombin may be prepared in sterile distilled water or isotonic saline. The intended use determines the strength of the solution to prepare. For general use in plastic surgery, dental extractions, skin grafting, neurosurgery, etc., solutions containing approximately 100 units per ml. are frequently used. For this, 10 ml. of diluent added to the 1,000 unit package is suitable. Where bleeding is profuse, as from cut surfaces of liver and spleen, concentrations as high as 1,000 to 2,000 units per ml. may be required. Intermediate strengths to suit the needs of the case may be prepared by selecting the proper strength package and dissolving the contents in an appropriate volume of diluent. In many situations, it may be advantageous to use THROMBOGEN Thrombin in dry form on oozing surfaces.

CAUTION: Solutions should be used immediately upon reconstitution. However, the solution may be refrigerated at 2–8°C, for up to three hours. The following techniques are suggested for the topical application of THROMBOGEN Thrombin.

1. The recipient surface should be sponged (not wiped) free of blood before THROMBOGEN Thrombin is applied.
2. A spray may be used or the surface may be flooded using a sterile syringe and small gauge needle. The most effective hemostasis results when the THROMBOGEN Thrombin mixes freely with the blood as soon as it reaches the surface.
3. In instances where THROMBOGEN Thrombin in dry form is needed, the vial is opened by removing the metal ring by flipping up the plastic cap and tearing counterclockwise. The rubber-diaphragm cap may be easily removed and the dried THROMBOGEN Thrombin is then broken up into a powder by means of a sterile glass rod or other suitable sterile instrument.
4. Sponging of treated surfaces should be avoided in order that the clot remain securely in place.
   THROMBOGEN Thrombin may be used in conjunction with Absorbable Gelatin Sponge, USP as follows:
   1. Prepare THROMBOGEN Thrombin solution of the desired strength.
   2. Immerse sponge strips of the desired size in the THROMBOGEN Thrombin solution. Knead the sponge strips vigorously with moistened gloved fingers to remove trapped air, thereby facilitating saturation of the sponge.
   3. Apply saturated sponge to bleeding area. Hold in place for 10 to 15 seconds with a pledget of cotton or a small gauze sponge.

THROMBOGEN Spray Kit: The THROMBOGEN Spray Kit contains one sterile vial of THROMBOGEN Thrombin, one sterile vial of isotonic saline diluent, one sterile disposable syringe and one sterile syringe spray tip. The kit may be used as follows:

1. Remove the Tyvek† blister lid from the outermost tray by pulling up at the indicated corner. The sterile inner tray can then be lifted out or introduced into the sterile field.
2. Remove the Tyvek† blister lid from the inner tray to expose the sterile contents.
3. Using the sterile syringe equipped with the needle, draw the desired amount of saline diluent from the vial into the syringe.
4. Inject the saline diluent into the THROMBOGEN Thrombin vial from the syringe to reconstitute the THROMBOGEN Thrombin powder.
5. When the THROMBOGEN Thrombin is completely dissolved, draw the THROMBOGEN Thrombin solution into the syringe.
6. Remove and discard the needle; affix spray tip by pushing down and turning clockwise until the spray tip locks in place.
7. Depress the syringe plunger in a normal fashion to dispense the THROMBOGEN Thrombin solution through the tip in a fine spray.
8. Alternatively, to facilitate using the THROMBOGEN Thrombin with an Absorbable Gelatin Sponge, USP, the THROMBOGEN Thrombin solution may be dispensed directly from the syringe into a sterile container vs. attaching the spray tip. When THROMBOGEN Thrombin is needed in the dry form, the vial is opened and the dried THROMBOGEN Thrombin pellet should be broken up into a powder with a sterile glass rod or other suitable instrument.

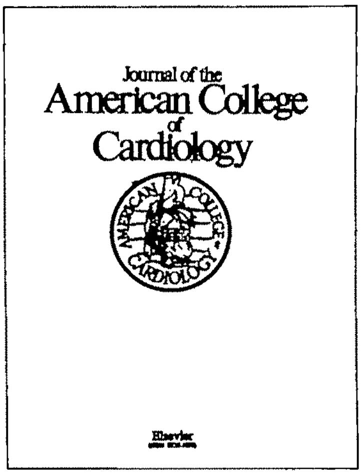
Caution: Federal law prohibits dispensing without a prescription.

THROMBOGEN Thrombin is manufactured by GenTrac, Inc.
Middleton, WI 53562
THROMBOGEN Thrombin is a trademark of
Johnson & Johnson Medical, Inc.
†Trademark of DuPont

Store at normal controlled room temperature, except 1000 unit vial of THROMBOGEN Thrombin, which must be stored between 2°-8°C (36°-46°F).

*TRADEMARK © JJM, INC. 1991 SSD 0675

Ten years of excellence
Journal of the American College of Cardiology


Journal of the American College of Cardiology
Elsevier

The Journal of the American College of Cardiology, JACC, is the leading journal in cardiology. **JACC's** timely coverage of clinically relevant information on the diagnosis and treatment of cardiovascular diseases has made it a favorite among cardiologists worldwide.

Why not join the thousands of your colleagues who have made reading **JACC** a part of their regular routine?

Read the **Journal of the American College of Cardiology** each month and you will find a superb collection of original articles, clinical reviews, special reports, and editorials at the forefront of cardiovascular medicine. **JACC's** comprehensive focus and distinguished editorial board assure you the most significant new information – information that you can apply directly to your practice.

Discover why **JACC** is the #1 journal in cardiology. Enter your subscription today and follow the most current and authoritative source on important developments in cardiology.

Journal of the American College of Cardiology
1992, Volumes 19, 20 (14 issues; 1 supplement)
ISSN **0735-1097**

Personal Rate: $94.00
Institutional Rate: $140.00
Intern/Resident/Nurse/Allied Health Rate: $58.00

For sample copies send to:
in North America
Elsevier Science Publishing Co., Inc.,
P.O. Box 882, Madison Square Station
New York, New York 10159

outside North America
Elsevier Science Publishers
P.O. Box 211, 1000 AE
Amsterdam, The Netherlands

Send subscription orders to your usual supplier or the New York address. For even faster service, call
Tel. No.: (212) 633-395
Fax No.: (212) 633-388

ELSEVIER
SCIENCE PUBLISHING COMPANY, INC.

10 YEARS OF SCIENTIFIC EXCELLENCE
10
JACC

8/91 XIE

THE ANNALS OF THORACIC SURGERY INFORMATION FOR AUTHORS

Thomas B. Ferguson, MD
Editor, *The Annals of Thoracic Surgery*
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

The Annals of Thoracic Surgery publishes original papers on topics in thoracic and cardiovascular surgery. Also featured are case reports, "how to do it" articles, classics in thoracic surgery, collective and current reviews, correspondence, and book reviews. All manuscripts, correspondence, and editorial business should be sent to the above address. Guidelines for collective and current reviews are available on request.

If a manuscript is accepted for publication, certain conditions must be agreed to by all authors. These include statements regarding conflict of interest, scientific responsibility, exclusive publication, and assignment of copyright. Elsevier Science Publishing Co, Inc, will maintain records of copyright for The Society. No part of the published material may be reproduced elsewhere without written permission from the publisher.

Because of escalating postage costs, manuscripts and illustrations will not routinely be returned to the authors. The editorial office will be responsible for proper disposal of the manuscripts so that confidentiality is preserved. Manuscripts and illustrations will be returned only if requested and a self-addressed stamped (US postage) envelope provided.

Checklist

The following checklist is provided for the author's convenience. Please utilize this list to make certain the manuscript is complete when submitted. Incomplete manuscripts cannot be accepted for editorial review.

General

☐ Submit original and *two* duplicate manuscripts (including three clearly separated and labeled sets of illustrations). Retain a fourth complete set as insurance against loss in the mail.

☐ Type manuscript double-spaced throughout (including title page, abstract, text, references, tables, and legends) on one side only on 22 × 28 cm (8½ × 11 inch) opaque bond paper with 3 cm (1¼ inch) margins all around. *This also applies to correspondence.* Type the last name of the first author in the upper right-hand corner of each page, including the title page.

☐ Arrange manuscript as follows: (1) title page, (2) abstract, (3) text, (4) references, (5) tables, and (6) legends. Number pages consecutively, beginning with the title page as page 1 and ending with the legend page.

☐ A manuscript for an *original article* ordinarily should not exceed 26 double-spaced typewritten pages, and should be proportionally shorter the more illustrations and tables that are included.

☐ The *text* for case reports should be *no more* than 4 double-spaced typewritten pages. If tables or illustrations are included, the text must be reduced. The text for a "how to do it" article should be even briefer, but with detailed illustrative material. Case reports and "how to do it" articles that exceed the allowable length will not be considered for publication.

☐ Referencing should be selective and pertain directly to the work being reported. Except in collective and current reviews, comprehensive listings serve no useful purpose and utilize valuable space. As a general guide, original articles should have no more than 20 references; case reports, 8 references; and "how to do it" articles, 5 references.

Title Page

☐ Give the paper as short a title as possible. Also submit a short title of 3 or 4 words to be used as a running head. Include only the names of the authors directly affiliated with the work, stating for each the single highest academic degree. Include the name and location of no more than two institutional affiliations.

☐ If the paper has been or is to be presented at the annual meeting of The Society of Thoracic Surgeons, the Southern Thoracic Surgical Association, or another scientific organization, provide a footnote giving the name, location, and dates of the meeting.

☐ At the bottom of the page, type "Address reprint requests to Dr . . ." followed by the last name, exact postal address with zip code, *telephone number, and FAX number* of the author to whom communications, proofs, and requests for reprints should be sent.

Abstracts

☐ Provide an abstract *no longer than 175 words* for an original article. Abstracts for case reports and "how to do it" articles should be shorter (50 to 75 words). An abstract must accompany *every* contribution, except for letters to the editor. Include several (3 to 5) keywords to assist in cross-indexing the article.

Text

☐ Generally, the text should be organized as follows: Introduction, Material and Methods, Results, and Comment.

☐ *Cite references, illustrations, and tables in numerical order* in the text. (Order of mention in text determines the number given to each.)

☐ Spell out, or define in parentheses, all abbreviations, even if they are commonly employed.

☐ Give all measurements and weights in *Système International (SI) units.* See "SI Unit Implementation—the Next Step" (JAMA 1988;260:73–6).

☐ For statistical nomenclature and data analysis, follow the "Guidelines for Data Reporting and Nomenclature" published in *The Annals of Thoracic Surgery* (1988;46:260–1) and found in the program book for the annual meeting of The Society of Thoracic Surgeons.

☐ Type footnotes at the bottom of the manuscript page on which they are cited. Credit suppliers of drugs, equipment, and other material described at length in the paper in footnotes, giving company name and location.

☐ Type acknowledgments, including complete grant or subsidy information, at the end of the text before the references.

References

☐ Identify references in the text using arabic numerals in parentheses on the line. Do not cite personal communications, manuscripts in preparation, and other unpublished data in the reference list. They may be mentioned in the text in parentheses.

☐ Type references double-spaced on a separate sheet. *Number consecutively in the order in which they are mentioned in the text.*

☐ Journal references should provide *inclusive* page numbers; book references should cite *specific* page numbers.

☐ Double-check references for accuracy, completeness, and nonduplication.

(Continued)

© 1992 by The Society of Thoracic Surgeons

☐ Abbreviations of journals should conform to those used in *Index Medicus*. The style and punctuation of the references should follow the formats outlined below:

Journal Article

8. Grillo HC, Suen HC, Mathisen DJ, Wain JC. Resectional management of thyroid carcinoma invading the airway. Ann Thorac Surg 1992;54:3–10.

(List *all* authors if 6 or fewer; otherwise list first 3 and add "et al.")

Chapter in Book

12. Vouhé PR. Transplantation of thoracic organs in children. In: Fallis JC, Filler RM, Lemoine G, eds. Pediatric thoracic surgery. New York: Elsevier, 1991:319–29.

Book (Personal Authors or Editors)

18. Shields TW, ed. Mediastinal surgery. Philadelphia: Lea & Febiger, 1991:1–10.

Tables

☐ Tables should be typewritten *double-spaced* on separate sheets, each with a table number (arabic) and title above the table and explanatory notes and legends below. Provide a key in alphabetical order to each table to identify all abbreviations used; this key should be placed below any explanatory notes.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published table(s).

☐ Tables should be self-explanatory, and the data should not be duplicated in the text or illustrations. If a table provides redundant information, it will be deleted.

Legends

☐ Type legends double-spaced on a single sheet. Numbers should be arabic and correspond to the order in which the illustrations occur in the text. Identify (in alphabetical order) all abbreviations appearing in the illustrations at the end of each legend. Give the type of stain and magnification power for all photomicrographs.

☐ Include written permission from *both the author and the publisher* to reproduce any previously published illustration(s).

☐ Enclose signed releases for recognizable (unmasked) photographs of human beings.

Illustrations

☐ Submit *triplicate* sets, each set in its own envelope, of *unmounted* and untrimmed black and white professionally prepared glossy prints. Components of the same illustration (eg, parts A and B) should be submitted separately. Photographs, rather than original art or photocopies, should be provided. All lettering should be done professionally and should be of adequate size to retain clarity after reduction (*final* lettering size in print should be 1.5 mm high). Illustrations will be reproduced at a width of one column (8.25 cm, 3¼ inches) or two columns (17.15 cm, 6¾ inches), or at an intermediate width ranging from 10.16 to 12.07 cm (4 to 4¾ inches).

☐ Many computer-generated illustrations are unsatisfactory for reproduction and should be professionally redrawn. Roentgenogram reproductions should be no smaller than 13 × 18 cm (5 × 7 inches).

☐ Place the first author's last name, the figure number, and an arrow indicating the *top* on a gummed label on the back of each illustration.

☐ If color illustrations are to be considered for publication, submit *both* positive 35-mm transparencies and color prints. Part of the printing costs for color illustrations will be borne by *The Annals*; however, the author must be prepared to pay $1,150 for the first color illustration on each page and $250 for every additional color illustration on the same page.

Human Investigation

☐ Include the date of approval by the local institutional human research committee or the ethical guidelines that were followed by the investigators in the Material and Methods section of the manuscript.

Humane Animal Care

☐ The Material and Methods section must contain a statement assuring that all animals have received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

Conflict of Interest

The Annals expects authors to disclose any commercial association that might pose a conflict of interest in connection with this manuscript. All funding sources supporting the work should be acknowledged in a footnote. Institutional or corporate affiliations of the authors that might constitute a conflict should be brought to the attention of the Editor.

Scientific Responsibility Statement

Before publication of an accepted manuscript, each author will be required to certify that he or she has participated sufficiently in the work to take responsibility for a meaningful share of the content of the manuscript, and that this participation included:

(a) conception or design of the experiment(s), or collection and analysis or interpretation of data;
(b) drafting the manuscript or revising its intellectual content; and
(c) approval of the final version of the manuscript to be published.

Exclusive Publication Statement

I certify that none of the material in this manuscript has been published previously, and that none of this material is currently under consideration for publication elsewhere. This includes symposia, transactions, books, articles published by invitation, and preliminary publications of any kind except an abstract of 400 words or fewer.

____

(Author's Signature)

Guidelines for the Submission of Electronic Manuscripts

☐ Please note that only the final accepted revision of a manuscript should be submitted as an electronic file. If you are planning to submit a manuscript in this format, please check box.

I. *Keyboarding of Manuscripts*

1) Our equipment can handle the following programs (any version) in their "native" format:

IBM Compatible

DisplayWrite
Executive Writer
Leading Edge
MicroSoft Word
Multimate
Office Writer
PC Write
PFS: Write
PFS: Professional
Q & A Write
Samna
Spellbinder
Volkswriter
WordPerfect
WordStar
WordStar 2000
Xywrite

Macintosh (do not use "Fast Save")

MacWrite
Microsoft Word
WordPerfect

Other word processors should be saved as ASCII files. For files saved as ASCII, consult the editorial office regarding the keyboarding of attributes such as bold, underline, superscript, subscript, etc.

2) All design considerations for typefaces, page layout, and artwork will be handled by the publisher after receipt of the electronic manuscript. **There is no need for the author to input special typesetting codes.**

3) Be especially sure to distinguish between the letters O and I and the numbers 0 and 1, respectively.

4) A "hard return" results from tapping the keyboard's **Enter** key. Use a hard return only to end a paragraph, or for titles, subheads, separate items on a list, etc. Rely on the word processor's word wrap ("soft return") within paragraphs, list items, etc.

5) Use your word processor's capabilities for the following text attributes:

- a) bold
- b) underline and italic
- c) subscript
- d) superscript
- e) strikeout

Text that will be italic in published form may be keyboarded italic or underlined.

6) **Do not use your word processor's hyphenation capabilities. Do not right justify text. Use two hyphens for long dashes.**

7) **In tables, use only tabs, not spaces, to align columns.**

II. *Organization and Delivery of Electronic Files*

1) Accepted manuscripts may be submitted on 3.5" or 5.25" diskettes, which must be either MS-DOS or Macintosh format. The author should retain copies of all files as backup. All diskettes must be accompanied by the *final* revision and a duplicate copy of the manuscript (including two clearly separated and labeled sets of illustrations) in full conformity with the standard Information for Authors on the preceding pages.

2) Diskettes should each be labeled with:

- a) author's name
- b) short title of article
- c) operating system
- d) format
- e) word processor used, including version number.

For example, DOS/DSDD/WordPerfect 4.2, or MAC/800K/MS Word v.3. Here, *DOS* and *Mac* indicate the operating system, *DSDD* (double-sided, double density) or *800K* indicates the diskette's physical format, and the remainder indicates the word processor used. Labels for your use are available from the Editorial Office.

3) If possible, it is helpful to have additional material such as tables, figure legends, and references saved as individual files—one file for each category. A file key should accompany the diskette.

4) Submit only the final accepted version of a manuscript. It is essential that submitted electronic files exactly match the final printout.

5) Diskettes should be packed between cardboard (or with foam or bubble-wrap) in an envelope that states that magnetic media is contained.

Please submit your word-processing diskette, the final revision and a duplicate copy of your manuscript, and two clearly separated and labeled sets of illustrations to:

Thomas B. Ferguson, MD
Editor
The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041

Telephone: (314) 361-6084
FAX: (314) 367-0585

© 1992 by The Society of Thoracic Surgeons

EVENTS OF INTEREST

Brief notices of meetings, courses, and symposia relevant to cardiothoracic surgery are published as a service. They should be formatted as follows: meeting title, date, place, sponsor, accreditation, director, fee, minimum/maximum attendance, and address/phone for further information. Announcements should be sent at least 4 months in advance of publication to *The Annals of Thoracic Surgery*, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110-1041; telephone, (314) 361-6084.

■ Specialty Review in Thoracic Surgery, Chicago, Illinois—January 11–16, 1993

For information on this review, sponsored by The National Center for Advanced Medical Education, contact the Registration Office, 707 S Wood St, Chicago, IL 60612; or call toll-free any time: 1-(800) 621-4651.

■ Introduction to Mitral Valve Surgery, Dallas, Texas—January 21–22, 1993

For information on this live teleconference, contact Lisa Turnbull, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 20 (facsimile: (714) 759-6911).

■ First International Symposium on Thoracoscopic Surgery, San Antonio, Texas—January 22–23, 1993

For information on this meeting, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons, San Antonio, Texas—January 25–27, 1993

For information on this meeting, contact Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; or telephone (312) 644-6610.

■ Third World Congress of the International Society of Cardio-Thoracic Surgeons, Salzburg, Austria—January 25–27, 1993

For information on this meeting, contact Prof Dr Felix Unger, c/o Interconvention, Austria Center Vienna, A-1450 Vienna, Austria; or telephone +43/1/23 69-26 43 (facsimile: +43/1/23 69-648).

■ Thirteenth Annual San Diego Cardiothoracic Surgery Symposium, San Diego, California—February 11–14, 1993

For information on this meeting, entitled "Pathophysiology & Techniques of Cardiopulmonary Bypass," contact CREF, PO Box 23220, San Diego, CA 92193; or telephone (619) 541-1444.

■ Forty-second Annual Meeting of the American College of Cardiology, Anaheim, California—March 14–18, 1993

For information on this meeting, contact American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814; or telephone (800) 253-4636.

■ Neurohumoral Effects of Profound Hypothermia in Infant Heart Surgery, London, England—March 18–19, 1993

For information on this meeting, contact The Postgraduate Centre, National Heart and Lung Institute, Dovehouse St, London SW3 6LY, England; or telephone 071-351 8172 (facsimile: 071-376 3442).

■ Le Club Mitrale, Paris, France—March 27–April 3, 1993

For information on this live teleconference, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 28 (facsimile: (714) 759-6911).

■ One Hundred Thirteenth Annual Meeting of the American Surgical Association, Baltimore, Maryland—April 1–3, 1993

For information on this meeting, contact American Surgical Association, Department of Surgery, CB 7245, University of North Carolina, 136 Burnett-Womack Building, Chapel Hill, NC 27599; or telephone (919) 966-4320 (facsimile: (919) 966-6009).

■ American College of Surgeons, Montreal, Canada—April 25–28, 1993

For information on this meeting, contact American College of Surgeons, 55 E Erie St, Chicago, IL 60611; or telephone (312) 664-4050 (facsimile: (312) 440-7014).

■ Seventy-third Annual Meeting of the American Association for Thoracic Surgery, Chicago, Illinois—April 26–28, 1993

For information on this meeting, contact American Association for Thoracic Surgery, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Fourteenth Annual Scientific Session of the North American Society of Pacing and Electrophysiology, San Diego, California—May 6–8, 1993

For information on this meeting, contact NASPE, 377 Elliot St, Newton Upper Falls, MA 02164; or telephone (617) 244-7300 (facsimile: (617) 244-3920).

■ 1993 World Symposium on Cardiomyoplasty and Biomechanical Assist, Paris, France—May 24–26, 1993

For information on this meeting, contact Beverly Farrier, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, extension 22 (facsimile: (714) 759-6911).

■ The International Society for Cardiovascular Surgery/The Society for Vascular Surgery, Washington, DC—June 7–9, 1993

For information on this meeting, contact the Association offices, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Fifth European Congress on Extra-Corporeal Circulation Technology, Arles, France, June 9–12, 1993

For information on this meeting, contact MOBO Promotions/FECECT, Catharijnesingel 105, 3511 GV Utrecht, Netherlands; or telephone 31-(0)30-310751 (facsimile: 31-(0)30-311198).

■ World Congress on Diseases of the Chest, Amsterdam, the Netherlands—June 13–18, 1993

For information on this meeting, contact XVII World Congress on Diseases of the Chest, International Academy of Chest Physicians & Surgeons, 3300 Dundee Rd, Northbrook, IL 60062-2348.

■ Nineteenth Annual Meeting of The Western Thoracic Surgical Association, Carlsbad, California—June 24–26, 1993

For information on this meeting, contact The Western Thoracic Surgical Association, 13 Elm St, Manchester, MA 01944; or telephone (508) 526-8330 (facsimile: (508) 526-4018).

■ Le Club Mitrale, Paris, France, June 26–June 3, 1993

For information on this live teleconference, contact Margo Irr, ProMedica International, 620 Newport Center Dr, Suite 575, Newport Beach, CA 92660; or telephone (714) 640-5870, ext 28 (facsimile: (714) 759-6911).

■ Twenty-first World Congress of The International Society for Cardiovascular Surgery, Lisbon, Portugal—September 12–15, 1993

For information on this meeting, contact ISCVS XXIst World Congress, Congress Secretariat, 13 Elm St, Manchester, MA 01944.

■ Neurological Injury and Pediatric Cardiac Surgery (including results of the prospective Boston Circulatory Arrest Study), Boston, Massachusetts, September 30–October 2, 1993

For information on this meeting, contact Laura Young, Department of Cardiac Surgery, Children's Hospital, 300 Longwood Ave, Boston, MA 02115; or telephone (617) 735-7930 (facsimile: (617) 735-6742).

■ Fifty-ninth Annual Scientific Assembly, American College of Chest Physicians, Orlando, Florida—October 24–28, 1993

For information on this meeting, contact American College of Chest Physicians, 3300 Dundee Rd, Northbrook, IL 60062; or telephone (708) 498-1400 (facsimile: (708) 498-5460).

■ Fortieth Annual Meeting of the Southern Thoracic Surgical Association, Panama City Beach, Florida—November 4–6, 1993

For information on this meeting, contact Southern Thoracic Surgical Association, 401 N Michigan Ave, Chicago, IL 60611-4267; or telephone (312) 644-6610 (facsimile: (312) 321-6869).

■ Sixty-sixth Scientific Session of the American Heart Association, Atlanta, Georgia, November 8–11, 1993

For information on this meeting, contact American Heart Association, 7320 Greenville Ave, Dallas, TX 75231; or telephone (214) 373-6300 (facsimile: (214) 373-3406).

Cardiovascular Surgeons All Over America Are Saying...

"Get My Booky®!"

See us in San Antonio (Booth #709) to find out which Booky® you need for your patients.

Booky® Cardiac Surgical Products

- **Flip Up Sternal Retractor**
- **Sternal Retractor Stabilizer**
- **Boomerang Cardiac Retractors**
- **Selective Sternal Retractor**

W.H. BOOKWALTER
AND ASSOCIATES, INC.
Booky® Cardiac Surgical Products
1-800-735-BOOK

US Postal Service Statement of Ownership, Management, and Circulation (Required by 39 USC 3685). 1A. Title of publication: The Annals of Thoracic Surgery. 1B. Publication No.: 026-320. 2. Date of filing: 11/1/92. 3. Frequency of issue: Monthly. 3A. No. of issues published annually: 12. 3B. Annual subscription price: $165.00 (Institutional), $95.00 (Personal). 4. Complete mailing address of known office of publication: Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. 5. Complete mailing address of the headquarters or general business offices of the publisher: The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611. 6. Full names and complete mailing address of publisher, editor, and managing editor: Publisher: The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611; Editor: Thomas B. Ferguson, MD, 3108 Queeny Tower, Barnes Hospital Plaza, St. Louis, MO 63110; Managing editor: Roger D. Morrison, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010. 7. Owner: The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611. 8. Known bondholders, mortgagees, and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages, or other securities: None. 9. The purpose, function, and nonprofit status of this organization and the exempt status for Federal income tax purposes have not changed during the preceding 12 months. 10. Extent and nature of circulation: A. Total No. copies: Average No. copies each issue during preceding 12 months: 11,332; Actual No. copies of single issue published nearest to filing date: 10,867. B. Paid and/or requested circulation: 1. Sales through dealers and carriers, street vendors, and counter sales: None. 2. Mail subscription: Average No. copies each issue during preceding 12 months: 9,036; Actual No. copies of single issue published nearest to filing date: 9,094. C. Total paid and/or requested circulation: Average No. copies each issue during preceding 12 months: 9,036; Actual No. copies of single issue published nearest to filing date: 9,094. D. Free distribution by mail, carrier, or other means, samples, complimentary, and other free copies: Average No. copies each issue during preceding 12 months: 502; Actual No. copies of single issue published nearest to filing date: 309. E. Total distribution: Average No. copies each issue during preceding 12 months: 9,538; Actual No. copies of single issue published nearest to filing date: 9,403. F. Copies not distributed: 1. Office use, left over, unaccounted, spoiled after printing: Average No. copies each issue during preceding 12 months: 1,794; Actual No. copies of single issue published nearest to filing date: 1,464. 2. Return from news agents: None. G. Total: Average No. copies each issue during preceding 12 months: 11,332; Actual No. copies of single issue published nearest to filing date: 10,867. 11. I certify that the statements made by me above are correct and complete.

Barry Glassberg

Barry Glassberg
Fulfillment Manager

FORTHCOMING ARTICLES

Original Articles

■ Argon Beam Coagulation Compared With Cryoablation of Ventricular Subendocardium

Paul J. Hendry, MD, Eileen M. Mikat, PhD, Mark P. Anstadt, MD, Mark D. Plunkett, MD, and James E. Lowe, MD

■ Benefits of Posttransplantation Monitoring of Interleukin 6 in Lung Transplantation

Yuichi Yoshida, MD, Yuichi Iwaki, MD, PhD, Si Pham, MD, James H. Dauber, MD, Samuel A. Yousem, MD, Adriana Zeevi, PhD, Shigeki Morita, MD, and Bartley P. Griffith, MD

■ Cerebral Metabolism and Circulatory Arrest: Effects of Duration and Strategies for Protection

James R. Mault, MD, Shigeaki Ohtake, MD, Mary E. Klingensmith, BA, Jeffrey S. Heinle, MD, William J. Greeley, MD, and Ross M. Ungerleider, MD

■ Component Analysis of Bilateral Anterior Cardiomyoplasty

Anthony P. Furnary, MD, James A. Magovern, MD, Ignacio Y. Christlieb, MD, Dennis R. Trumble, and George J. Magovern, MD

■ Effects of University of Wisconsin Solution on Coronary Artery Endothelium-Dependent Relaxation in the Rat

Raymond Cartier, MD, Charleen Hollmann, RN, François Dagenais, MD, Josie Buluran, BSc, Michel Pellerin, MD, and Yves Leclerc, MD

■ Homograft Aortic Root Replacement for Destructive Prosthetic Endocarditis

Harinder Singh Bedi, MCh, and Alan E. Farnsworth, FRCS(Ed)

■ Human Cryopreserved Allografts: Electron Microscopic Analysis of Cellular Injury

Donald G. Crescenzo, MD, Stephen L. Hilbert, PhD, Robert H. Messier, Jr, MD, Patrick W. Domkowski, MS, Mary Kay Barrick, BS, Perry L. Lange, BS, Victor J. Ferrans, MD, PhD, Robert B. Wallace, MD, and Richard A. Hopkins, MD

■ Hyperbaric Oxygenation for Arterial Air Embolism During Cardiopulmonary Bypass

Shahar Kol, MD, Ron Ammar, MD, Giora Weisz, MD, and Yehuda Melamed, MD

■ Improved Multiorgan Function After Prolonged Univentricular Support

J. Michael Duncan, MD, Clay M. Burnett, MD, O. H. Frazier, MD, Michael S. Sweeney, MD, J. David Vega, MD, and Branislav Radovancevic, MD

■ Skeletal Muscle Ventricles: Left Ventricular Apex to Aorta Configuration

Huiping Lu, MD, Robert Fietsam, Jr, MD, Robert L. Hammond, BA, Hidehiro Nakajima, MD, Frank W. Mocek, MD, Gregory A. Thomas, MD, Rene Ruggiero, MD, Hisako Nakajima, MD, Michael Colson, MS, and Larry W. Stephenson, MD

■ Total Anomalous Pulmonary Venous Connection in Neonates and Young Infants: Repair in the Current Era

Adnan Cobanoglu, MD, and Victor D. Menashe, MD

■ Warm Blood Cardioplegia: Superior Protection After Acute Myocardial Ischemia

W. Morris Brown III, MD, John L. Jay, MD, John Parker Gott, MD, Alice H. Huang, PhD, Pan-Chih, MD, W. Stewart Horsley, MD, Lynne M. A. Dorsey, BS, MBA, Sara Katzmark, BS, Robert J. Siegel, MD, and Robert A. Guyton, MD

Case Reports

■ Multiple Tumor Emboli After Pneumonectomy

David D. Spencer, DO, Jorge L. de la Garza, MD, and William A. Walker, MD

■ Treatment of Incessant Reciprocating Atrioventricular Tachycardia by a Closed Heart Surgical Technique

Yves A. Louagie, MD, Luc De Roy, MD, and Jean-Claude Schoevaerdts, MD

How to Do It

■ Simplified Method for Delivering Normothermic Blood Cardioplegia

Philippe Menasché, PhD, Bernard Touchot, MD, Frédéric Pradier, DPharm, Gérard Bloch, MD, and Armand Piwnica, MD

Classics in Thoracic Surgery

■ Naming the Bronchopulmonary Segments and the Development of Pulmonary Surgery

Will C. Sealy, MD, Samuel R. Connally, PhD, and Martin L. Dalton, MD

Current Review

■ Solitary Squamous Cell Papilloma of the Trachea

Yoshifumi Naka, MD, Kazuyasu Nakao, MD, Yasumasa Hamaji, MD, Masaaki Nakahara, MD, Masahiko Tsujimoto, MD, and Kazuya Nakahara, MD

World Symposium Cardiomyoplasty Biomechanical Assist and Artificial Heart

LE PALAIS DES CONGRÈS DE PARIS
PARIS, FRANCE

MAY 24-26, 1993

THE SCIENTIFIC COMMITTEE

Alain Carpentier, M.D., Ph.D., Chairman (France)

Juan Carlos Chachques, M.D. (France)

Valerij Chekanov, M.D. (Russia)

Ray C-J Chiu, M.D., Ph.D., FRCS, FACS (Canada)

Adib Jatene, M.D. (Brazil)

George Magovern, M.D. (USA)

Philippe Mikaeloff, M.D. (France)

Dirk Pette, M.D. (Germany)

Stanley Salmons, M.Sc., Ph.D. (England)

Albert Starr, M.D. (USA)

Larry Stephenson, M.D. (USA)

World Symposium Cardiomyoplasty Biomechanical Assist and Artificial Heart

MAY 24-26, 1993

PLEASE PRINT OR TYPE

☐ Send Information

☐ Register Me

Name: First Last M.D., Prof., R.N. Companion

Mailing Address Hospital

City State Zip Country

Telephone Fax Specialty

Mail to: ProMedica International • 620 Newport Center Drive, Suite 575 • Newport Beach, CA 92660 • USA
Contact: Margo Irr • TEL (714) 640-5870 Ext 28 • FAX (714) 759-6911

Fontan Procedure for Hypoplastic Left Heart Syndrome

William I. Norwood, Jr, MD, PhD, Marshall L. Jacobs, MD, and John D. Murphy, MD
The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

Since 1985, 354 neonates have undergone palliative reconstruction for hypoplastic left heart syndrome with 109 early deaths and 12 late deaths. Of the survivors, before 1989, 77 patients underwent a subsequent modified Fontan operation, consisting of baffling the atrial septal defect to the tricuspid valve (initial 25 patients) or intra-atrial baffling of the inferior vena cava to the pulmonary arteries and superior vena cava (52 patients). There were 17 early deaths and three late deaths. Major serous effusions developed in 42 patients (54%) after Fontan operation. Since 1989, a staged approach to Fontan's operation was undertaken in an effort to reduce the volume load of the right ventricle as early as possible, to minimize the impact of rapid changes in ventricular geometry and diastolic function that can accompany a primary Fontan operation, and to reduce effusive complications. Thus, at a mean age of 6 months, 121 patients have undergone closure of aortopulmonary shunt, augmentation of central pulmonary arteries, and association of the superior vena cava with the branch pulmonary arteries (hemi-Fontan procedure). Of these, 61 patients have already undergone completion of the Fontan procedure with six early deaths and three late deaths. Major serous effusions developed in 28 patients (46%) with the staged Fontan. For perspective, the contemporary experience since January 1991 consists of 58 neonates who have undergone initial palliation with 11 deaths (19%), 17 patients who have undergone the hemi-Fontan procedure with one death (6%), and 21 patients who have undergone completion of the Fontan operation with one death (5%). In conclusion, a total of 138 patients with hypoplastic left heart syndrome have undergone Fontan's procedure. A two-stage approach to total cavopulmonary connection has not eliminated the transient morbidity of serous effusions but has been associated with a significant improvement in patient survival ($p < 0.05$).

(Ann Thorac Surg 1992;54:1025–30)

In the early 1970s, Fontan and Baudet [1] and Kreutzer and associates [2] independently introduced operative treatment of tricuspid atresia that produced nearly normal oxygen saturation of the systemic circulation and normal volume work for the systemic ventricle. Since that time, the principle of the Fontan operation has been applied to a variety of heart malformations with a single functional ventricle [3]. At an estimated prevalence of 1 to 4 per 10,000 live births, hypoplastic left heart syndrome (HLHS) is the most common defect with one functional ventricle. It accounts for 7% to 8% of congenital heart disease seen in the first year of life, and it is the most common cause of death due to heart disease in the newborn period [4].

The reconstructive surgical approach to HLHS is based on the principle that carefully planned and appropriately timed palliative operations should result in physiology suitable for repair by a modification of the Fontan procedure. The normally high pulmonary vascular resistance of the neonate precludes the possibility of achieving a cavopulmonary connection, and thus separating the systemic and pulmonary circulations, as a reparative procedure shortly after birth. Thus, a standardized surgical approach to HLHS in the neonate has evolved based on initial palliation, which consists of atrial septectomy, transection of the main pulmonary artery, anastomosis of the proximal main pulmonary artery to the diminutive ascending aorta, augmentation of the ascending aorta and entire aortic arch with excision of the contraductal shelf, and construction of a systemic to pulmonary artery shunt. The initial palliative procedure is embodied by three basic principles: (1) the aorta must be associated directly with the right ventricle in a fashion that guarantees unobstructed flow from the right ventricle to the systemic circulation with growth potential obviating a further aortic operation; (2) pulmonary blood flow must be regulated for proper growth and development and maturation of the pulmonary vasculature to avoid the development of pulmonary vascular obstructive disease and to minimize the volume load on the ventricle; and (3) a large interatrial communication is necessary to avoid pulmonary venous hypertension.

After initial palliation, the systemic and pulmonary circulations are connected at the arterial level, and the volume work of the single ventricle is equal to the sum of the systemic and pulmonary blood flow. After a period of maturation of the pulmonary vasculature, systemic venous return may be directed to the pulmonary arteries,

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Norwood, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd, Philadelphia, PA 19104.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

thus placing the systemic and pulmonary circulations in series, reducing the volume work of the right ventricle to the equivalent of the systemic blood flow only and achieving a more normal systemic arterial oxygen saturation. Successful physiologic repair of HLHS by completion of the Fontan operation in a previously palliated infant was first reported by Norwood and associates in 1983 [5].

The purpose of the present study was to analyze the surgical results and clinical outcome for patients with HLHS treated by a staged approach to surgical reconstruction culminating in a modified Fontan procedure. Previous reports from this institution have dealt with the short-term and intermediate-term results of the initial reconstructive operation [6, 7], the hemodynamic assessment after the initial reconstructive operation and its relevance to the modified Fontan procedure [8], and the outcome of a modified Fontan procedure for HLHS as the second and final stage of reconstruction [9]. At The Children's Hospital of Philadelphia, recent efforts to improve the overall outcome of operation for HLHS have included the division of the Fontan procedure into two stages: the hemi-Fontan procedure, wherein the systemic to pulmonary artery shunt is closed and the superior vena cava is associated with the branch pulmonary arteries, and the completion Fontan procedure, wherein the inferior vena cava is associated with the superior vena cava and pulmonary arteries. The specific focus of this study is to evaluate the effect of this two-stage approach to the Fontan operation for HLHS on morbidity and mortality.

Material and Methods

Patients

The medical records of 138 consecutive patients treated with some modification of the Fontan procedure who initially underwent a reconstructive operation for HLHS at The Children's Hospital of Philadelphia between January 1985 and September 1991 were retrospectively reviewed, including echocardiographic records, cardiac catheterization reports, surgical notes, and hospital charts. For purposes of analysis, the patients were divided into two cohorts: those who underwent a primary Fontan operation after initial palliative reconstruction, and those who were managed by a two-staged approach to the Fontan operation (hemi-Fontan followed by completion Fontan). Comparisons of survival after the modified Fontan operation were made between cohorts using Fisher's exact test [10].

Operative Technique

For the hemi-Fontan procedure, extracorporeal circulation is accomplished by cannulation of the neoaorta and the right atrium. Hypothermic cardiopulmonary bypass is established using a bubble oxygenator with integrated heat exchanger. The polytetrafluoroethylene systemic to pulmonary artery shunt is occluded using metallic clips as soon as bypass has been established. Flow is maintained at approximately 150 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} until nasopharyngeal and esophageal temperatures are less than 18°C. The ascending aorta is cross-clamped. The circulation is discontinued, and blood is drained into the oxygenator-reservoir through the venous cannula. A single dose of cold crystalloid cardioplegia solution is infused into the aortic root. The pulmonary arteries are freed from behind the aorta, and a longitudinal incision is made in the anterior aspect of the pulmonary arteries extending from the level of origin of the right upper lobe branch to the level of origin of the left upper lobe branch. An incision is made in the most superior portion of the right atrium and is extended onto the medial aspect of the superior vena cava (Fig 1A). At the most rightward extent of the pulmonary arteriotomy, the right pulmonary artery is anastomosed to the posterior lip of the opened superior vena cava (Fig 1B). A gusset of cryopreserved pulmonary artery homograft is used to augment the confluence of the pulmonary arteries and to create a roof over the patulous anastomosis of the pulmonary arteries to the superior vena cava (Fig 1C). A portion of the same homograft gusset is used as a dam to close the junction of the right atrium with the superior vena cava (Fig 1D). The heart is then recannulated.

For the completion Fontan, cannulation and bypass are accomplished in identical fashion. After administration of cardioplegia and during hypothermic circulatory arrest, the lateral wall of the right atrium is opened longitudinally, anterior and parallel to the sulcus terminalis. The incision extends inferiorly to the level of the eustacian valve of the inferior vena cava and superiorly to within a few millimeters of the junction of the right atrium with the superior vena cava. A portion of the pulmonary artery homograft that had been used as a dam to close the right atrium–superior vena cava junction is excised, taking care that the resulting orifice is as large as the inferior vena cava. A gusset of appropriate length is then cut from a portion of a 10-mm polytetrafluoroethylene tube graft that has been opened longitudinally. This is then used to create a lateral atrial tunnel by which inferior vena caval flow is directed to the pulmonary arteries (Fig 2). A portion of the tunnel comprises the free wall of the right atrium. This partitioning of the atrium is fundamentally similar to techniques previously described by de Leval [11], Puga [12], Norwood [13], and others. After closure of the atriotomy incision, reperfusion and rewarming and separation from bypass are accomplished. Catheters are inserted for the postoperative measurement of pressures within the atrium and the systemic venous pathway.

Results and Comment

From January 1985 to September 1991, 354 neonates underwent initial palliative reconstruction for HLHS at The Children's Hospital of Philadelphia, with 109 early deaths and 12 late deaths. A systematic review of the outcome of initial palliation was reported in 1990 by Murdison and associates [14]. The early (less than 30 days) mortality rate was 33.5%. Analysis revealed that survival was related neither to the anatomical subtype of HLHS nor to the type of aortopulmonary shunt that was constructed. One third of all deaths occurred due to cardiovascular collapse during the first postoperative day.

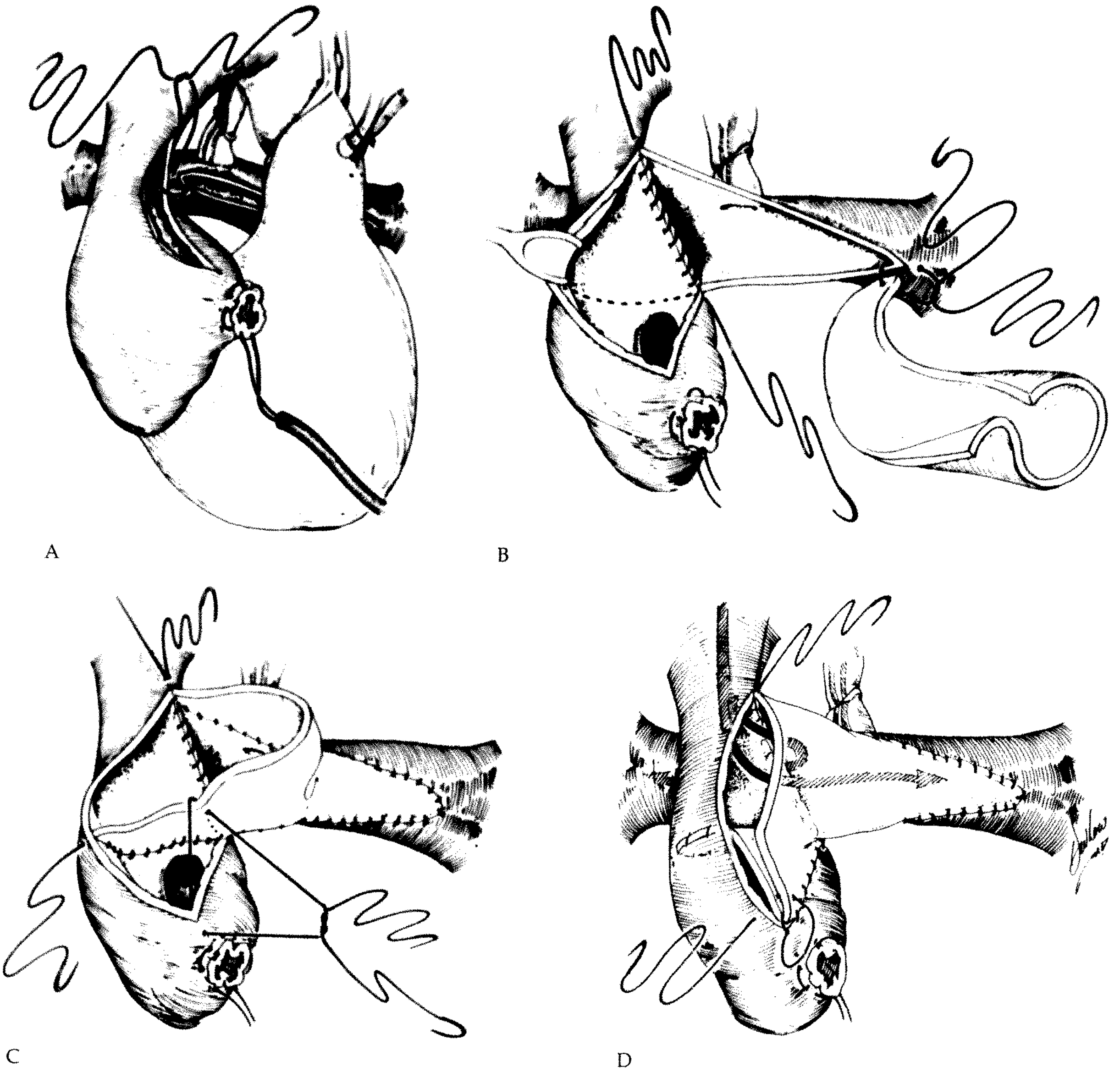


Fig 1. The hemi-Fontan procedure: (A) A longitudinal incision is made in the anterior aspect of the pulmonary arteries extending from the level of origin of the right upper lobe branch to the level of origin of the left upper lobe branch. An incision is made in the most superior portion of the right atrium and is extended onto the medial aspect of the superior vena cava. (B) At the most rightward extent of the pulmonary arteriotomy, the right pulmonary artery is anastomosed to the posterior lip of the opened superior vena cava. (C) A gusset of cryopreserved pulmonary artery homograft is used to augment the confluence of the pulmonary arteries and to create a roof over the patulous anastomosis of the pulmonary arteries to the superior vena cava. (D) A portion of the same homograft gusset is used as a dam to close the junction of the right atrium with the superior vena cava. The shaded arrow *indicates the path of flow of blood from the superior vena cava into the right and left pulmonary arteries.*

Analysis of this early mortality suggested that successful postoperative management depends on the maintenance of a critical balance between systemic and pulmonary blood flow. This flow ratio is related directly to the ratio of systemic and pulmonary vascular resistances. It appears that carbon dioxide has a potent and relatively independent influence on pulmonary vascular resistance, making possible some clinical control over this physiology by manipulation of the degree of mechanical ventilation. Recently, the initial postoperative management has been modified to include the routine addition of carbon dioxide to the inspired gas mixture [15, 16]. This allows more precise control of the relative resistances in the systemic and pulmonary vascular beds, while maintaining normal minute ventilation, and has virtually eliminated cardiovascular collapse in the very early postoperative period. Thus, from January to September 1991, 58 neonates underwent initial palliation with 11 deaths (mortality, 19%).

The staged approach to reconstructive operation for HLHS is directed toward eventual separation of the systemic and pulmonary circulations by the application of the Fontan procedure. Before 1989, 77 survivors of initial palliation underwent a subsequent modified Fontan operation. In the initial 25 patients, the procedure included

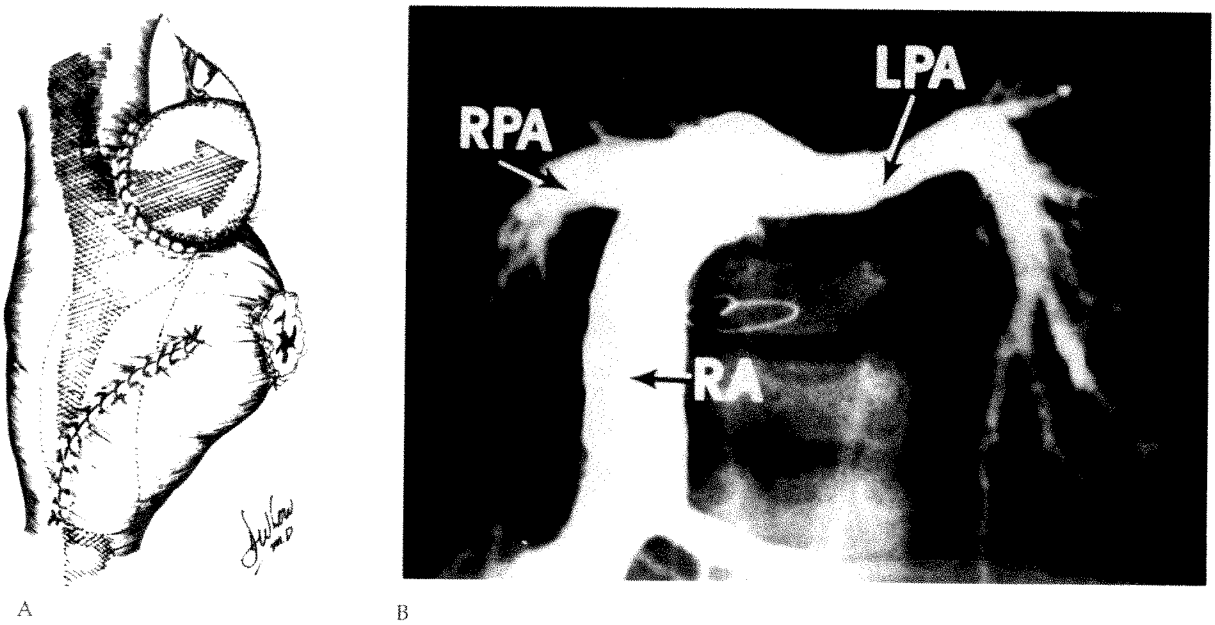


Fig 2. The completion Fontan procedure: (A) The completed cavopulmonary connection. After excision of the portion of pulmonary artery homograft that was used as a dam to close the right atrium–superior vena cava junction, the inferior vena cava is associated with the confluence of the superior vena cava and pulmonary arteries by atrial partitioning, which is accomplished with a gusset of polytetrafluoroethylene. (B) A single frame of a cineangiogram of the systemic venous pathway obtained during follow-up cardiac catheterization after completion Fontan procedure. (LPA = *left pulmonary artery;* RA = *the systemic venous pathway through the partitioned right atrium;* RPA = *right pulmonary artery.)*

baffling of the atrial septal defect to the tricuspid valve, and in the subsequent 52 patients, intraatrial baffling of the inferior vena cava to the pulmonary arteries and superior vena cava. The patients ranged in age from 5 months to 6 years (median age, 19 months). There were 17 early deaths and three late deaths. A detailed review of this series of patients was reported recently by Farrell and associates [8]. There were no detectable differences in intermediate survival rates after a modified Fontan procedure among the anatomic subtypes of HLHS. Chang and colleagues [9] from this institution previously reported their evaluation of the relation of preoperative hemodynamic parameters to the outcome of a modified Fontan procedure in patients with HLHS. They analyzed preoperative "risk factors" including elevated pulmonary artery pressure (mean pulmonary artery pressure >15 mm Hg), elevated pulmonary vascular resistance (>4 U · m^2), elevated ventricular end-diastolic pressure (>12 mm Hg), pulmonary artery distortion, and tricuspid regurgitation of moderate or severe degree. There was no statistical difference in percent mortality for any of these factors, although there was a trend toward poorer outcome in the presence of moderate or severe tricuspid regurgitation. This did not achieve statistical significance, as the number of patients with moderate or severe tricuspid regurgitation (n = 7) was small. Analysis of preoperative hemodynamics does not predict which patients are at risk for ventricular dysfunction and death after a Fontan procedure. It is nonetheless true that in some patients, an unpredictable and rapid decrease in ventricular diastolic volume accompanies closure of the systemic to pulmonary artery shunt and diversion of systemic venous blood to the pulmonary arteries, and this is associated with marked changes in ventricular geometry that result in markedly diminished ventricular compliance, elevated atrial and pulmonary artery pressures, low cardiac output, tachycardia, and eventual death.

Cardiac catheterization of survivors of the Fontan procedure for HLHS has revealed excellent function of the right ventricle as the systemic ventricle [8]. Nonetheless, a high percentage of patients experienced postoperative morbidity related to the occurrence of serous effusions. Forty-two of the 77 patients (54%) who underwent a primary Fontan procedure after initial palliation had development of major pleural or pericardial effusions or ascites.

Since 1989, a staged approach to the Fontan operation was undertaken in an effort to reduce the volume load of the right ventricle as early as possible, to minimize the impact of rapid changes in ventricular geometry and diastolic function that can accompany a primary Fontan operation, and to reduce effusive complications. Thus, at a mean age of 6 months, 121 patients have undergone a hemi-Fontan procedure [17]. This comprises closure of the systemic to pulmonary artery shunt, augmentation of the central pulmonary arteries, and association of the superior vena cava with the branch pulmonary arteries. The pattern of blood flow achieved after a hemi-Fontan operation is essentially the same as that achieved by a more conventional "bidirectional" Glenn procedure. We believe that certain technical features of the hemi-Fontan operation make it a more logical step in the process of achieving eventual completion of the Fontan procedure. First, it includes the elimination of any areas of stenosis or distortion of the branch pulmonary arteries and their confluence. Second, the normal relation of the superior vena cava to the right atrium is preserved, considerably simplifying the eventual completion of the Fontan procedure and obviating the need for reestablishing the connection of the superior vena cava to the right atrium. Instead, a portion of the homograft dam is merely excised, leaving a widely patent opening between the right atrium and the confluence of the superior vena cava with the pulmonary arteries.

Between August 1989 and September 1991, 61 patients have undergone completion of the Fontan operation after a previous hemi-Fontan procedure. There have been six early deaths and three late deaths. This represents a significant improvement in patient survival ($p < 0.05$). Once again, serous effusions represent the most prevalent morbid complication in this group of patients. Major serous effusions developed in 28 of 61 patients after the staged Fontan procedure. The majority of the 52 survivors (follow-up period, 1 month to 25 months) were described by their cardiologists as doing well from both a cardiovascular and a developmental standpoint. The oldest girl wears glasses, captains the kickball team, and receives A's and B's in standard fifth-grade class. Approximately two thirds of the children (35 patients) take no medications. The remainder take digoxin alone or in combination with a diuretic. One patient has had recurrent supraventricular tachyarrhythmias. One patient underwent pacemaker implantation for temporary atrioventricular dissociation but is now in normal sinus rhythm.

Conclusions

So far, a total of 138 patients with HLHS have undergone the Fontan procedure. Cardiac catheterization of survivors reveals excellent function of the right ventricle as the systemic ventricle. A two-stage approach to the Fontan operation, including a hemi-Fontan procedure at 6 months of age followed by completion Fontan procedure at 12 to 18 months, has not eliminated the transient morbidity of serous effusions, but has been associated with a significant improvement in patient survival ($p < 0.05$).

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8.
2. Kreutzer GO, Vargas FJ, Schlichter AJ, et al. Atriopulmonary anastomosis. J Thorac Cardiovasc Surg 1972;83:427–36.
3. Marcelletti C, Mazzera E, Olthof H, et al. Fontan's operation: an expanded horizon. J Thorac Cardiovasc Surg 1980;80:764–9.
4. Fyler DC. Report of the New England Regional Infant Cardiac Program. Pediatrics 1980;65(Suppl):463.
5. Norwood WI, Lang P, Hansen DD. Physiologic repair of aortic atresia—hypoplastic left heart syndrome. N Engl J Med 1983;308:23–6.
6. Pigott JD, Murphy JD, Barber G, Norwood WI. Palliative reconstructive surgery for hypoplastic left heart syndrome. Ann Thorac Surg 1988;45:122–8.
7. Murphy JD. Hypoplastic left-heart syndrome in children. Curr Opin Pediatr 1991;3:803–9.
8. Farrell PE, Chang AC, Murdison KA, Baffa JM, Norwood WI, Murphy JD. Outcome and assessment after the modified Fontan procedure for hypoplastic left heart syndrome. Circulation 1992;85:116–22.
9. Chang AC, Farrell PE, Murdison KA, et al. Hypoplastic left heart syndrome: hemodynamic and angiographic assessment after initial reconstructive surgery and relevance to modified Fontan procedure. J Am Coll Cardiol 1991;17:1143–9.
10. Matthews DE, Farewell V. Using and understanding medical statistics. Basel: Karger, 1985:20–38.
11. De Leval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. J Thorac Cardiovasc Surg 1988;96:88:908–13.
12. Puga FJ, Chiavarelli M, Hagler DJ. Modifications of the Fontan operation applicable to patients with left atrioventricular valve atresia or single atrioventricular valve. Circulation 1987;76(Suppl 3):53–9.
13. Norwood WI Jr. Hypoplastic left heart syndrome. Ann Thorac Surg 1991;52:688–95.
14. Murdison KA, Baffa JM, Farrell PE Jr, et al. Hypoplastic left heart syndrome. Outcome after initial reconstruction and before modified Fontan procedure. Circulation 1990;82(Suppl 4):199–207.
15. Jacobs ML, Murphy JD, Nicolson SC, Steven JM, Norwood WI. Manipulation of inspired carbon dioxide in neonates with one ventricle and systemic-to-pulmonary artery shunt. Circulation 1991;84(Suppl 2):238.
16. Jobes DR, Nicolson SC, Steven JM, Miller M, Jacobs ML, Norwood WI Jr. Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome. Ann Thorac Surg 1992;54:150–1.
17. Baffa JM, Rychik J, Gullquist SD, et al. Outcome following bidirectional cava-pulmonary anastomosis prior to modified Fontan procedure. J Am Coll Cardiol 1991;17:33A.

DISCUSSION

DR HILLEL LAKS (Los Angeles, CA): The award of the Maxwell Chamberlain Memorial Paper to this report is a fitting tribute to a major advance in the treatment of a highly lethal common disease in neonatal cardiac surgery. It is also a fitting sequel to the same group's Maxwell Chamberlain paper of 1987, five years ago, in which the results of the first-stage Norwood procedure were described.

For those inclined to make major advances to the field of cardiac surgery, a major challenging problem, preferably one considered insoluble, must be chosen. Hypoplastic left heart syndrome, a term coined by Noonan and Nadas in 1958, was considered until the early 1980s, and in some centers to this day, a lesion with a hopeless prognosis even with surgical intervention.

Once a major problem has been chosen, advances in this treatment require ability, creativity, and perseverance. Dr Norwood and his colleagues first at The Children's Hospital in Boston and, subsequently, at the Philadelphia Children's Hospital over the last 10 years have developed original surgical techniques, methods of postoperative care, and strategies of staging that have resulted in a marked improvement in the results of surgical therapy.

The results of the first stage have improved from a mortality of 30% to 19% in 1991. The early mortality for the Fontan performed as a second stage was 22% and has now fallen to 10% when performed as a third stage. To compare the results of a three-stage approach with that of other methods, such as transplantation, one needs to look at a cohort of patients diagnosed at birth and then followed up for 5 or 10 years with all deaths included, both preoperative and postoperative throughout the follow-up period. It was unclear from reading the manuscript what the overall mortality for the three-stage approach is in this experience.

Taking the best-case scenario, which Dr Jacobs has shown us, the initial palliation of mortality of 19%, hemi-Fontan of 6%, and Fontan of 5%, which are their 1991 statistics, give an overall mortality of 29%. This does not include the late mortality for each of the three stages, which if we assume is 15% on the basis of previous reports, would give us an overall mortality in the range of 44%.

Dr Jacobs, are those estimations are in accordance with your experience?

The results of cardiac transplantation I have were kindly supplied by Leonard Bailey's group at Loma Linda. They have 46 patients who actually underwent transplantation who had a mortality while waiting of 30%, an operative mortality of 11%, and a late mortality of 7%, giving an overall mortality, if one includes all groups, of 47%, including the waiting period, with a 1-year survival for the entire neonatal heart transplant experience of 84%. This 47% may not be significantly different than that described by the three-stage approach, although one must assume that the mortality while waiting does not include those deaths before referral to Loma Linda.

I have a question with regard to the second stage procedure. In the absence, Dr Jacobs, of demonstrable pulmonary artery stenosis by angiography, must one use cardiopulmonary bypass and circulatory arrest for what is in essence a bidirectional Glenn shunt? In our own experience we have been able to do the bidirectional Glenn shunt in the majority of patients without the use of bypass using a temporary superior vena cava to right atrial shunt.

With regard to the Fontan procedure, or third stage, how many patients died while waiting for the stage and what were the criteria for acceptance for a Fontan procedure? Was there a correlation in your recent experience with risk factors and mortality? You mentioned that in the previous experience there was no correlation with the risk factors; however, although there was no statistically significant difference, there was a difference in mortality with a higher mortality in the high-risk groups.

With regard to the high incidence of serous effusions, why have you not incorporated the partial Fontan, either using the adjustable atrial septal defect or the fenestrated Fontan, which the Boston group has shown to reduce the incidence of postoperative effusions?

I would like once again to congratulate the authors of this study on their wonderful pioneering work in finding solutions to a very difficult surgical problem.

DR JACOBS: Thank you, Dr Laks, for your very kind comments. I will do my best to answer the several questions that you posed. First of all, I appreciate your summation of the mortality associated with the staged approach to surgical reconstruction, as that is very helpful to the audience. The staged approach to the Fontan operation, wherein the volume load on the ventricle is reduced earlier in life, has resulted in a significant reduction of the interval mortality between first-stage palliation and completion of the Fontan operation. The figures that I presented included both operative mortality and late mortality at each of the three stages, and when summed, they do represent a very close approximation of the total mortality for this treatment plan at the present time.

We, as others, are very excited about the approach that Dr Bailey and his colleagues have taken to the management of infants with hypoplastic left heart syndrome. Reconstructive surgery and replacement surgery have both been demonstrated to have important roles in the management of what was previously considered an untreatable and uniformly lethal disease. I think that in comparing the outcome of the two approaches, it is important to recognize that our experience at The Children's Hospital of Philadelphia deals with a very nonselected group of patients. Virtually all of the neonates who are referred to us for initial palliative reconstruction are included in the analysis that I presented. As a result of the screening process before acceptance for transplantation, and then the possibility of death before referral or while awaiting transplantation, it is very possible that the outcome statistic that Dr Laks presented for the Loma Linda transplant experience represents a highly selected patient group. Thus, it is not possible to compare the outcome of these two very different treatment plans on the basis of surgical mortality alone.

As to your question regarding the conduct of the second-stage procedure, and specifically the utility of cardiopulmonary bypass and hypothermic circulatory arrest, it is our belief that the hemi-Fontan operation as described has certain advantages over a conventional "bidirectional Glenn" procedure as a step in a process toward achieving eventual completion of the Fontan procedure. As noted, it includes the elimination of any areas of stenosis or distortion of the branch pulmonary arteries and their confluence. Thus, the potential need for pulmonary arterioplasty at the time of completion Fontan is obviated. Second, the normal relation of the superior vena cava to the right atrium is preserved, considerably simplifying the eventual completion of the Fontan procedure and obviating the need for reestablishing the connection of the superior vena cava to the right atrium. Finally, regarding the question about the incidence of serous effusions and the potential impact of fenestration of the interatrial baffle, we too have explored this possibility, based on the very encouraging results from both Dr Laks' group at Los Angeles and Dr Castaneda's group in Boston. In our experience, this modification has not had a significant impact on the incidence or severity of serous effusions. Of the group of patients undergoing completion Fontan for hypoplastic left heart syndrome, 10 were left with an adjustable communication in the atrial baffle. Of these 10 patients who underwent the Fontan operation with a fenestration or adjustable atrial septal defect, 5 (50%) experienced major effusions.

I hope I have addressed all of Dr Laks' questions, and thank him again for his comments. We are honored to have had the opportunity to present the Maxwell Chamberlain Memorial Paper, and grateful for the privilege of addressing The Society.

Aprotinin Therapy for Reoperative Myocardial Revascularization: A Placebo-Controlled Study

Delos M. Cosgrove III, MD, Blaine Heric, MD, Bruce W. Lytle, MD, Paul C. Taylor, MD, Roberto Novoa, MD, Leonard A. R. Golding, MD, Robert W. Stewart, MD, Patrick M. McCarthy, MD, and Floyd D. Loop, MD

Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio

We tested the efficacy and safety of aprotinin in 169 patients undergoing isolated reoperative myocardial revascularization. Patients were randomly assigned to high-dose aprotinin, low-dose aprotinin, or placebo treatment groups in a double-blind, placebo-controlled study. Treatment groups did not differ significantly with respect to age, sex, red cell mass, number of grafts, use of internal thoracic artery, or incidence of preoperative aspirin therapy. Patients treated with aprotinin had a significant reduction in postoperative chest tube drainage (720 ± 753, 866 ± 1,636, and 1,121 ± 683 mL, respectively, for high-dose aprotinin, low-dose aprotinin, and placebo; $p < 0.001$). Transfusion requirements were reduced in aprotinin-treated patients (2.1 ± 4.2, 4.8 ± 11.8, and 4.1 ± 6.2 units for high-dose, low-dose, and placebo, respectively; $p < 0.001$). A similar reduction in chest tube drainage and transfusion requirements was seen in patients using aspirin preoperatively. Q-wave myocardial infarctions were increased in the aprotinin subgroups (17.5%, 14.3%, and 8.9% for high-dose, low-dose, and placebo groups; not significant). Acute vein graft thrombosis was found in six of 12 vein grafts studied at postmortem examination in patients receiving aprotinin but not in any of five grafts in patients receiving placebo. We conclude that aprotinin is extremely effective in reducing bleeding and transfusion requirements and may increase the risk of graft thrombosis.

(Ann Thorac Surg 1992;54:1031–8)

Bleeding during and after a cardiac operation is a common problem that carries a major risk of early and late complications. Royston and associates [1] first observed that aprotinin decreased bleeding and transfusion requirements after cardiopulmonary bypass in patients undergoing myocardial revascularization. Numerous authors have confirmed this observation in primary operations and in patients receiving aspirin preoperatively [2–16]. Previous studies have reported few adverse effects attributable to the use of aprotinin. Reoperative myocardial revascularization poses a significantly greater challenge for surgeons in achieving hemostatic control [17]. Thus, we sought to determine whether aprotinin would reduce bleeding, transfusion requirements, and complications of bleeding in reoperative myocardial revascularization.

Material and Methods

From January 1990 through June 1991, 169 patients undergoing isolated reoperative myocardial revascularization were prospectively entered into a randomized, double-blind, placebo-controlled study with aprotinin stratified into two dosage levels. High-dose aprotinin consisted of 70 mg of aprotinin in 50 mL of 0.9% saline solution; low-dose aprotinin consisted of 35 mg of aprotinin in 50 mL of 0.9% saline solution. The placebo contained only 50 mL of saline solution. The trial drug was provided by the manufacturer.

After induction of anesthesia, a loading dose of 200 mL of the test solution was given intravenously through the central venous catheter over 20 minutes. Immediately after this, a continuous infusion of 50 mL/h was begun and maintained until the patient left the operating room. An additional 200 mL of the test drug was added to the prime volume of the cardiopulmonary bypass machine.

Before cardiopulmonary bypass was initiated, the patient was heparinized with 300 IU/kg. Activated clotting times were recorded at regular intervals. Additional heparin was administered if clotting times fell to less than 400 seconds. At the conclusion of cardiopulmonary bypass, heparin was reversed with protamine sulfate at a dosage of 1 mg/100 IU of heparin administered. Residual heparin was monitored with activated clotting times.

The demographic and preoperative characteristics of the three treatment groups were not significantly different (Table 1). The operative procedure was remarkably similar for the three groups except for time required for closure of the patient, which was statistically longer for patients who did not receive aprotinin (Table 2).

Primary results consist of comparisons between the aprotinin and placebo groups. High-dose and low-dose aprotinin groups were combined for these comparisons. The χ^2 or Fisher's exact tests were used to test for aprotinin effects in categorical data. Because much of the

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Cosgrove, Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Characteristics of 169 Patients Undergoing Isolated Reoperative Myocardial Revascularization and Treated With High-Dose Aprotinin, Low-Dose Aprotinin, or Placebo

Characteristic	High Dose (n = 57)	Low Dose (n = 56)	Placebo (n = 56)	p Value[a]
Age	60.8 ± 7.8	61.1 ± 8.3	63.0 ± 8.8	NS
Males	50 (87.7%)	45 (80.4%)	49 (87.5%)	NS
Mean no. of previous operations	1.1 ± 0.4	1.1 ± 0.3	1.1 ± 0.4	NS
Operations (>1)	6 (10.5%)	5 (8.9%)	7 (12.5%)	NS
Years postop	9.6 ± 3.6	9.4 ± 4.5	8.7 ± 3.3	NS
Red cell mass (mL)	2,308.8 ± 399.7	2,200.8 ± 393.1	2,154.4 ± 429.4	NS
Preop aspirin	17 (29.8%)	7 (12.5%)	12 (21.4%)	NS

[a] Tests for statistical significance compare aprotinin versus placebo.

NS = not significant.

continuous data failed to meet normality assumptions, the nonparametric Wilcoxon rank sums test was used to make group comparisons for continuous variables. Pairwise differences between high-dose, low-dose, and placebo groups were of secondary interest. Overall differences were examined with the χ^2 or Fisher's exact tests (categorical data) or Kruskal-Wallis tests (continuous data). Where the overall test indicated significant between-group differences, pairwise comparisons between the three treatment groups were made. Because of the increased risk of type I error due to multiple comparisons, a p value of less than 0.01 was considered significant for these pairwise comparisons.

The presence of perioperative Q-wave myocardial infarction was determined from electrocardiographic recordings by an outside observer who was blinded to the therapy.

Results

Patients receiving aprotinin had significantly less postoperative chest tube drainage than controls, both for the first 8 hours and for the entire time that chest tubes were in place. Reduced drainage was also found in the subgroup of patients receiving preoperative aspirin therapy. Although there was a trend toward less bleeding in patients receiving high-dose aprotinin as opposed to low-dose aprotinin in the aspirin subgroup, this trend was not significant (Table 3).

Transfusion requirements were reduced in patients receiving aprotinin and in those patients taking aspirin. This reduction was caused in part by the reduced percentage of patients requiring any transfusion at all. The trend and the magnitude of the influence are similar in the entire group and in those patients taking aspirin (Table 4).

Additional evidence corroborating the improvement in hemostasis for the aprotinin groups came from the requirement for other hemostatic agents. ϵ-Aminocaproic acid was given to 23% of the patients in the placebo group, to 4% of the high-dose, and to 2% of the low-dose aprotinin patients, respectively. The difference in incidence of administration between the aprotinin patients and placebo patients was statistically significant ($p < 0.01$).

Operative mortality for the entire group was 8% and did not differ between subgroups. The incidence of perioperative Q-wave myocardial infarction was increased in patients receiving aprotinin, but the increase was not statistically significant. Median serum glutamic-oxaloacetic transaminase level showed a similar but not significant trend. The percentage of patients with increases in creatinine level greater than 44.2 μmol/L (0.5 mg/dL) was greater in the high-dose than in the low-dose or placebo groups but was not significant (Table 5).

Postmortem examinations were obtained in 7 of the 13 patients who died during the study. Particular attention was given to graft patency (Table 6). Thrombi were found in six of 12 vein grafts in 9 patients receiving aprotinin. Five vein grafts in 4 patients receiving placebo were patent. All internal thoracic and gastroepiploic arteries were patent at the time of postmortem examination.

Table 2. Comparison of Surgical Variables for the Aprotinin and Placebo Treatment Groups

Surgical Variable	High Dose	Low Dose	Placebo	p Value[a]
Grafts per patient	2.8 ± 0.9	3.3 ± 0.9	3.1 ± 1.2	NS
Internal thoracic artery	34 (59.7%)	34 (60.7%)	30 (53.6%)	NS
Closure time (min)	71.6 ± 26.9	74.3 ± 37.7	89.9 ± 36.9	<0.0001
Operation time (h)	5.1 ± 1.5	5.6 ± 1.6	5.4 ± 1.4	NS

[a] Tests for statistical significance compare aprotinin versus placebo.

NS = not significant.

Comment

Postoperative hemorrhage necessitating reexploration or homologous blood transfusions is a major source of mortality and early and late morbidity after reoperative coronary artery bypass grafting. In a series of 1,500 consecutive coronary artery reoperations performed at The Cleveland Clinic Foundation since 1967, the incidence of reexploration was 7% [17]. Blood conservation techniques that can minimize transfusion requirements in patients undergoing cardiac operations include autologous blood predonation, prebypass collection of autologous blood and platelet-rich plasma, use of crystalloid oxygenator prime, perioperative blood salvage, autotransfusion techniques [18], fibrin glue, and pharmacologic therapy [1–20]. Pharmacologic agents that affect postoperative hemorrhage include desmopressin acetate [21–23], ϵ-aminocaproic acid [24], tranexamic acid [25], and aprotinin [16]. Aprotinin is a serine protease and kallikrein inhibitor with an extraordinary ability to preserve platelet function and inhibit fibrinolysis [26]. The efficacy of aprotinin in reducing postoperative blood loss by approximately 50% has been established in multiple randomized studies, primarily performed in Europe [1–16]. The encouraging results of these studies turned our attention to aprotinin use in reoperative patients who are at especially high risk for postoperative blood loss.

We found that patients undergoing reoperative myocardial revascularization who received aprotinin had a statistically significant reduction in blood loss and a reduced need for blood transfusion when compared with the placebo-controlled group. The high-dose aprotinin, low-dose aprotinin, and placebo groups were similar in regard to previously established independent predictors of blood use, including mean red cell volume, age, and preoperative aspirin use [27, 28]. The reduction in postoperative blood loss and the percentage of patients transfused was similar in both the high-dose and low-dose aprotinin groups, although the mean number of units transfused was similar for the low-dose and the placebo groups. These findings confirm the results of European randomized studies, the majority of which were performed in patients undergoing primary myocardial revascularization.

Table 3. Chest Tube Drainage for Aprotinin Study Groups and for Patients Receiving Aspirin

Variable	High Dose	Low Dose	Placebo	p Value[a]
Entire group (n = 169)				
No. of patients	57	56	56	NS
Drainage				
First 8 hours	229 ± 196	293 ± 268	487 ± 270	0.002
Total	720 ± 753	866 ± 1636	1,121 ± 683	0.0001
Patients taking aspirin				
No. of patients	17	7	12	NS
Drainage				
First 8 hours	275 ± 273	271 ± 140	577 ± 386	0.001
Total	688 ± 620	870 ± 697	1,092 ± 492	0.02

[a] Tests for statistical significance compare aprotinin versus placebo.

NS = not significant.

Table 4. Transfusion Requirements for Patients and Number of Patients Transfused in Each Group

Variable	High Dose	Low Dose	Placebo	p Value[a]
Entire group (n = 169)				
No. of patients	57	56	56	NS
Red cells (U)	2.1 ± 4.2	4.8 ± 11.8	4.1 ± 6.2	0.001
Platelets (U)	1.6 ± 6.3	3.3 ± 15.4	5.4 ± 14.6	0.006
Patients transfused	26 (45.6%)	29 (51.8%)	44 (78.6%)	0.001
Patients taking aspirin (n = 36)				
No. of patients	17	7	12	NS
Red cells (U)	1.9 ± 3.3	3.7 ± 2.9	3.8 ± 2.6	0.03
Patients transfused	8 (47.1%)	5 (71.4%)	12 (100%)	0.006

[a] Tests for statistical significance compare aprotinin versus placebo.

NS = not significant.

These same studies have shown aprotinin to be generally safe with few serious complications. Complications with the use of aprotinin include allergic reactions manifested by apparent histamine-mediated cardiovascular collapse [29–32], renal toxicity [33], heparin resistance [34], and potentiation of the effects of muscle relaxants [35]. We observed no significant allergic complications or drug interactions in our study. Horl [36] reviewed multiple animal studies and found that aprotinin has effects on renal perfusion and glomerular filtration rate that are secondary to its effects on renin prostaglandin metabolism and on the kallikrein kinin system. Fisher and Knupfer [37], in another review of animal studies, found aprotinin to have minimal effects on renal function, although adverse effects had been seen with high doses under hypothermic conditions. Multiple clinical studies of renal function after use of high-dose aprotinin have not shown clinically adverse effects [1, 5]. In contrast, our study demonstrated a small dose-related increase in serum creatinine level in the aprotinin-treated group. This increase did not appear to be clinically significant; however, it remains a concern.

Of greater concern is the increase in myocardial infarction rates observed in both the high-dose and low-dose aprotinin groups compared with the control group. Graft thrombosis secondary to aprotinin-induced reduction in fibrinolysis and enhanced platelet aggregation has long been a concern of surgeons using aprotinin in prospective studies; however, this potential complication has not yet been observed or documented, despite the wide use of aprotinin in patients undergoing primary myocardial revascularization.

The most likely cause of myocardial infarction in the aprotinin-treated patients is graft occlusion secondary to thrombus. Three sources of data support this concern.

Table 5. Morbidity and Mortality Results for Each Aprotinin Study Group

Variable	High Dose	Low Dose	Placebo	*p* Value[a]
Mortality	4 (7.0%)	5 (8.9%)	4 (7.1%)	NS
MI	9 (15.8%)	5 (8.9%)	4 (7.1%)	NS
Reop for bleeding	1 (1.8%)	3 (5.4%)	0 (0%)	NS
Creatinine increase >0.5 mg/dL	14 (24.6%)	11 (19.6%)	10 (17.9%)	NS
Creatinine clearance (mL/min)	132.9 ± 77.8	122.0 ± 61.5	110.7 ± 46.5	NS
Median SGOT (IU/L)	93.0	92.0	79.5	NS

[a] Tests for statistical significance compare aprotinin versus placebo.

MI = myocardial infarction; NS = not significant; SGOT = serum glutamic-oxaloacetic transaminase.

First is the demonstrated 50% saphenous vein graft thrombosis rate seen in our aprotinin-treated, autopsied patients. Second is the report of early formation of thrombi on pulmonary artery catheters in cardiac surgical patients receiving high-dose aprotinin [38, 39]. Third is the experimental evidence that aprotinin is protective in mediating the effect of myocardial ischemia and limiting infarct size. In one study the kallikrein inactivating effect of aprotinin limited myocardial ischemic injury in dogs undergoing coronary occlusions [40]. This protective effect of aprotinin has been demonstrated in other studies [41–52] and has led to its use as a cardioplegia additive [53, 54]. The myocardial protective effect of aprotinin has also led to its beneficial use in weaning patients from an intraaortic balloon pump after coronary revascularization [55]. These data suggest that the mechanism of action of aprotinin in our patients who experienced myocardial infarctions is not related to any direct deleterious effect on the myocardium but is caused by the mechanical consequences of a hypercoagulable state and subsequent graft occlusions. Thus, we might expect that aprotinin-treated patients undergoing nonrevascularization procedures might be relatively protected from this complication.

Unique pathologic characteristics of our reoperative patients may have contributed to their increased myocardial infarction rates. Reoperative candidates, in contrast to those undergoing primary revascularizations, often have smaller target coronary arteries with more tenuous collateral flow and more severe coronary atherosclerosis. These features of the coronary circulation might make our "borderline" conduits more susceptible to low flow, stasis, and clot propagation in the hypercoagulable state that might be created by aprotinin. Another possible explanation is that aprotinin increases activated clotting time in a dose-related fashion and decreases heparin therapy for cardiopulmonary bypass [56–59], which may have led to our inadequately anticoagulating some of our patients. The absence of clot formation in the bypass circuit or other thromboembolic complications in our study group does not support this explanation.

Table 6. Incidence of Patency Among 21 Grafts From Seven Postmortem Examinations

Graft Source	Aprotinin	Placebo	*p* Value
Veins	6 (50%)	5 (100%)	0.10
Internal thoracic artery	3 (100%)	0	NA
Gastroepiploic artery	1 (100%)	0	NA

NA = not applicable.

An additional finding of our study is the reduction in transfusion requirements in those patients who received aspirin preoperatively. Previous studies have found a significant increase in postoperative bleeding and blood product requirements in patients maintained on aspirin preoperatively [60, 61]. The number of patients transfused was reduced from 100% in the placebo group to 67% and 40% in the high-dose and low-dose groups, respectively. These findings confirm those of Bidstrup and associates [62], who found that 44 patients undergoing primary aortocoronary bypass operations after aspirin therapy had a reduction in chest tube drainage from 1,393 mL to 352 mL and a significantly reduced transfusion requirement from 2.7 units per patient in the control group to 0.8 units per patient in the aprotinin group. This "aspirin neutralizing" effect of aprotinin has also been demonstrated in a canine model in which bolus treatment with aprotinin reversed the prolonged bleeding times produced by the interactive effects of recumbent tissue-type plasminogen activator and aspirin [63].

The amplified effect of aprotinin in reversing the antiplatelet effects of aspirin is fundamentally related to the mechanism of action of aprotinin. Aspirin-induced acetylation of platelet cyclooxygenase inhibits thromboxane synthesis. Thromboxane A_2 is a potent stimulator of platelet aggregation, and its reduction in aspirin-treated patients may account for the increased bleeding times observed in this group. Nagaoka and associates [64] found an improved prostaglandin metabolism and platelet aggregation in aprotinin-treated patients undergoing cardiopulmonary bypass. This ability to preserve platelet aggregation properties via its effects on platelet membrane receptors may account for aprotinin's dramatic effects in reducing bleeding in our aspirin-pretreated group.

It is evident that aprotinin dramatically alters coagulation in patients undergoing cardiopulmonary bypass. The evidence of vein graft thrombosis raises the question of a hypercoagulable state that may adversely influence patient outcome. There is also a suggestion that bleeding complications and blood requirements as well as thrombotic complications are dose-related. A dose-response curve has been established for aprotinin's effect on activated clotting times. As the mechanism of action of this drug is more clearly determined, it may be possible to develop a treatment regimen that both prevents the coagulopathy associated with cardiopulmonary bypass and avoids potential thrombotic complications.

References

1. Royston D, Bidstrup BP, Taylor KM, Sapsford RN. Effect of aprotinin on need for blood transfusion after repeat open-heart surgery. Lancet 1987;2:1289–91.
2. Blauhut B, Gross C, Necek S, Doran JE, Spath P, Lundsgaard-Hansen P. Effects of high-dose aprotinin on blood loss, platelet function, fibrinolysis, complement, and renal function after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1991;101:958–67.
3. Harder MP, Eijsman L, Roozendaal KJ, van Oeveren W, Wildevuur CRH. Aprotinin reduces intraoperative and postoperative blood loss in membrane oxygenator cardiopulmonary bypass. Ann Thorac Surg 1991;51:936–41.
4. Locatelli A, Maurelli M, Bianchi T, et al. Aprotinin in cardiac surgery [Letter]. Lancet 1991;338:254.
5. Van Oeveren W, Jansen NJG, Bidstrup BP, et al. Effects of aprotinin on hemostatic mechanisms during cardiopulmonary bypass. Ann Thorac Surg 1987;44:640–5.
6. Alajmo F, Calamai G, Perna A, et al. High-dose aprotinin: hemostatic effects in open heart operations. Ann Thorac Surg 1989;48:536–9.
7. Bidstrup BP, Royston D, McGuinness C, Sapsford RN. Aprotinin reduces bleeding in patients taking aspirin at the time of open heart surgery [Abstract]. Circulation 1989; 80(Suppl 2):158.
8. Commin PL, Lu H, Soria C, Caen JP. Mechanisms of bleeding reduction induced by aprotinin during cardiopulmonary bypass: a controlled study [Abstract]. Anesthesiology 1990; 73:A1205.
9. Carrel T, Bauer E, Laske A, von Segesser L, Turina M. Low-dose aprotinin for reduction of blood loss after cardiopulmonary bypass [Letter]. Lancet 1991;337:673.
10. Royston D, Bidstrup B. Reduction in postoperative blood loss in patients having open heart reoperations using high dose aprotinin (Trasylol) [Abstract]. Anesthesiology 1987;67:A23.
11. Dietrich W, Barankay A, Dilthey G, et al. Reduction of homologous blood requirement in cardiac surgery by intraoperative aprotinin application: clinical experience in 152 cardiac surgical patients. Thorac Cardiovasc Surg 1989;37: 92–8.
12. Fraedrich G, Weber C, Bernard C, Hettwer A, Schlosser V. Reduction of blood transfusion requirement in open heart surgery by administration of high doses of aprotinin: preliminary results. Thorac Cardiovasc Surg 1989;37:89–91.
13. Dietrich W, Spannagl M, Jochum M, et al. Influence of high-dose aprotinin treatment on blood loss and coagulation patterns in patients undergoing myocardial revascularization. Anesthesiology 1990;73:1119–26.
14. Naorose-Abidi SM, Bond LR, Chitolie A, Bevan DH. Desmopressin therapy in patients with acquired factor VIII inhibitors [Letter]. Lancet 1988;1:366.
15. Havel M, Teufelsbauer H, Knobl P, et al. Effect of intraoperative aprotinin administration on postoperative bleeding in patients undergoing cardiopulmonary bypass operation. J Thorac Cardiovasc Surg 1991;101:968–72.
16. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
17. Lytle BW, Loop FD, Cosgrove DM, et al. Fifteen hundred coronary reoperations: results and determinants of early and late survival. J Thorac Cardiovasc Surg 1987;93:847–59.
18. Cosgrove DM, Amiot DM, Meserko JJ. An improved technique for autotransfusion of shed mediastinal blood. Ann Thorac Surg 1985;40:78–9.
19. Estafanous FG, Cosgrove DM. Blood conservation and utilization. In: Estafanous FG, ed. Anesthesia and the heart patient. Boston: Butterworths, 1989:165–70.
20. Scott WJ, Kessler R, Wernly JA. Blood conservation in cardiac surgery. Ann Thorac Surg 1990;50:843–51.
21. Seear MD, Wadsworth LD, Rogers PC, Sheps S, Ashmore PG. The effect of desmopressin acetate (DDAVP) on postoperative blood loss after cardiac operations in children. J Thorac Cardiovasc Surg 1989;98:217–9.
22. Hackmann T, Gascoyne RD, Naiman SC, et al. A trial of desmopressin (1-desamino-8-D-arginine vasopressin) to reduce blood loss in uncomplicated cardiac surgery. N Engl J Med 1989;321:1437–43.
23. Salzman EW, Weinstein MJ, Weintraub RM, et al. Treatment with desmopressin acetate to reduce blood loss after cardiac surgery. N Engl J Med 1986;314:1402–6.
24. Vander Salm TJ, Ansell JE, Okike ON, et al. The role of ε-aminocaproic acid in reducing bleeding after cardiac operation: a double-blind randomized study. J Thorac Cardiovasc Surg 1988;95:538–40.
25. Horrow JC, Hlavacek J, Strong MD, et al. Prophylactic tranexamic acid decreases bleeding after cardiac operations. J Thorac Cardiovasc Surg 1990;99:70–4.
26. Emerson TE. Pharmacology of aprotinin and efficacy during cardiopulmonary bypass. Cardiovasc Drug Rev 1989;7: 127–40.
27. Ferraris VA, Gildengorin V. Predictors of excessive blood use after coronary artery bypass grafting. A multivariate analysis. J Thorac Cardiovasc Surg 1989;98:492–7.
28. Cosgrove DM, Loop FD, Lytle BW, et al. Determinants of blood utilization during myocardial revascularization. Ann Thorac Surg 1985;40:380–4.
29. Bohrer H, Bach A, Fleischer F, Lang J. Adverse haemodynamic effects of high-dose aprotinin in a paediatric cardiac surgical patient. Anaesthesia 1990;45:853–4.
30. Proud G, Chamberlain J. Anaphylactic reaction to aprotinin. Lancet 1976;2:48–9.
31. Levy AH. Unusual reaction to Trasylol [Letter]. Can Med Assoc J 1974;111:1304.
32. McMahon MJ, Axon ATR. Anaphylactic reaction to aprotinin [Letter]. Br J Med 1984;289:1696.
33. Fischer JH. Effects of Trasylol on the kidneys: dependence on temperature and dose. In: Dudziak R, Reuter HD, Kirchhoff PG, Schumann F, eds. Proteolysis and proteinase inhibition in cardiac and vascular surgery. Stuttgart: Schattauer Verlag, 1985:127–35.
34. Gersbach PH, Lammle B, Schupbach P, Muhlemann W, Althaus U. Major coagulation disorders when using aprotinin: observations on a case. Thorac Cardiovasc Surg 1991;39: 196–8.
35. Chasapakis G, Dimas C. Possible interaction between muscle relaxants and the kallikrein-trypsin inactivator "Trasylol." Br J Anaesth 1966;38:838–9.
36. Horl WH. Effect of aprotinin on renal function. In: Dudziak R, Reuter HD, Kirchhoff PG, Schumann F, eds. Proteolysis and proteinase inhibition in cardiac and vascular surgery. Stuttgart: Schattauer Verlag, 1985:137–42.
37. Fischer JH, Knupfer P. High-dose aprotinin (Trasylol) therapy: harmless to the kidney? Langenbecks Arch Chir 1983; 360:241–9.
38. Bohrer H, Fleischer F, Lang J, Vahl C. Early formation of thrombi on pulmonary artery catheters in cardiac surgical patients receiving high-dose aprotinin. J Cardiothorac Anesth 1990;4:222–5.

39. Youngberg JA. Aprotinin and thrombus formation on pulmonary artery catheters: a piece of the coagulation puzzle. J Cardiothorac Anesth 1990;4:155–8.
40. Diaz PE, Fishbein MC, Davis MA, Askenazi J, Maroko PR. Effect of the kallikrein inhibitor aprotinin on myocardial ischemic injury after coronary occlusion in the dog. Am J Cardiol 1977;40:541–9.
41. Okamura T, Walls JT, Rovetto MJ, Curtis J, Higgenbotham C. Aprotinin enhanced myocardial function and ATP levels after normothermic and hypothermic ischemia [Abstract]. Circulation 1986;74(Suppl 2):68.
42. Hartmann JR, Robinson JA, Gunnar RM. Chemotactic activity in the coronary sinus after experimental myocardial infarction: effects of pharmacologic interventions on ischemic injury. Am J Cardiol 1977;40:550–5.
43. Miller AG, Mustafa SJ, Glenn TM. Protection of the regionally ischemic left ventricle by aprotinin. Pharmacologist 1976; 18:192.
44. Yokoyama M, Miyamoto H, Fujiwara H, Sunamori M, Suzuki A. The effect of pharmacological pretreatment on the long term global ischemic heart: myocardial enzyme activity and lysosomes. J Mol Cell Cardiol 1985;17:70.
45. Hallett MB, Shandall A, Young HL. Mechanism of protection against "reperfusion injury" by aprotinin. Roles of polymorphonuclear leucocytes and oxygen radicals. Biochem Pharmacol 1985;34:1757–61.
46. Krug A. Animal-experimental investigations on the effect of Trasylol on the sequelae of a temporary coronary artery occlusion on the myocardium. In: Cantin M, Haberland GL, Schnells G, Selye H, eds. New aspects of Trasylol therapy. Stuttgart: Schattauer Verlag, 1975:43–8.
47. Eisenbach J, Heine H. Effect of the proteinase inhibitor Trasylol on the mortality and infarct size in dogs with acute myocardial infarction. Pharmacol Res Commun 1977;9:79–92.
48. Tanaka H, Sunamori M, Amano J, Nakagawa T, Suzuki A. Effect of protease inhibitor "aprotinin" on reperfused ischemic myocardium [Abstract]. J Mol Cell Cardiol 1987; 19(Suppl 1):543.
49. Lefer AM, Spath JA Jr. Protective effect of protease inhibition in myocardial ischemia. In: Cantin M, ed. New aspects of Trasylol therapy; vol 8: Experimental myocardial infarction. Int Symp Duesseldorf. Stuttgart: Schattauer Verlag, 1975: 311–28.
50. Wilkens HJ, Steger R, Back N. Effect of the protease inhibitor Trasylol in acute coronary occlusion in dogs. In: Cantin M, ed. New aspects of Trasylol therapy; vol 8: Experimental myocardial infarction. Int Symp Duesseldorf. Stuttgart: Schattauer Verlag, 1975:381–92.
51. Hartmann J, Fareed J, Messmore H, Robinson J, Gunnar R. Postinfarct fibrinolytic activity: inhibition by Trasylol [Abstract]. Am J Cardiol 1976;37:13748R.
52. Napolitano D, Ruggiero A, Cuomo A, Improta M. Treatment of the syndrome of myocardiac infarction with an inhibitor of the proteinases. In: Donatelli L, ed. Proteases and antiproteases in cardioangiology. Stuttgart: Schattauer Verlag, 1969: 135–44.
53. Sunamori M, Innami R, Amano J, Suzuki A, Harrison CE. Role of protease inhibition in myocardial preservation in prolonged hypothermic cardioplegia followed by reperfusion. J Thorac Cardiovasc Surg 1988;96:314–20.
54. Hjelms E, Waldorff S, Steiness E, Bergsten O. Aprotinin does not add protective effect to cold cardioplegia during coronary artery bypass surgery. Scand J Thorac Cardiovasc Surg 1986;20:11–3.
55. Sunamori M, Suzuki A. Improved efficacy of intra-aortic balloon pumping by pharmacological myocardial protection for postoperative pump failure after coronary revascularization. Jpn J Surg 1988;18:61–7.
56. DeSmet AAEA, Joen MCN, van Oeveren W, et al. Increased anticoagulation during cardiopulmonary bypass by aprotinin. J Thorac Cardiovasc Surg 1990;100:520–7.
57. Von Segesser LK, Weiss BM, Pasic M, et al. Experimental evaluation of heparin-coated cardiopulmonary bypass equipment with low systemic heparinization and high-dose aprotinin. Thorac Cardiovasc Surg 1991;39:251–6.
58. Davies RJ, Lane DA, McGregor IR, Preston FE. The neutralisation of heparin by Trasylol. Thromb Res 1980;17:533–7.
59. Shikimi T. Immunochemical and kinetic evidence that heparin enhances aprotinin activity. Jpn J Pharmacol 1985;38: 433–5.
60. Ferraris VA, Ferraris SP, Lough FC, Berry WR. Preoperative aspirin ingestion increases operative blood loss after coronary artery bypass grafting. Ann Thorac Surg 1988;45:71–4.
61. Taggart DP, Siddiqui A, Wheatley DJ. Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. Ann Thorac Surg 1990;50:425–8.
62. Bidstrup BP, Royston D, McGuinness C, Sapsford RN. Aprotinin in aspirin-pretreated patients. Perfusion 1990; 5(Suppl):77–81.
63. Garabedian HD, Gold HK, Leinbach RC, et al. Bleeding time prolongation and bleeding during infusion of recombinant tissue-type plasminogen activator in dogs: potentiation by aspirin and reversal with aprotinin. J Am Coll Cardiol 1991; 17:1213–22.
64. Nagaoka H, Innami R, Murayama F, et al. Effects of aprotinin on prostaglandin metabolism and platelet function in open heart surgery. J Cardiovasc Surg 1991;32:31–7.

DISCUSSION

PROF KENNETH M. TAYLOR (London, England): I should like first to compliment Dr Heric and his colleagues on their presentation in this important area of blood conservation. Their results confirm our initial findings regarding the efficacy of aprotinin therapy, particularly in reoperations. In the original Hammersmith study, blood loss in reoperations was reduced from 1,500 mL to 300 mL.

The Cleveland data showed a reduction from 1,120 to 720 mL. I suggest, however, that Dr Heric's data may underestimate the reduction in blood loss in the high-dose aprotinin group because they measured drainage loss rather than hemoglobin loss due to their protocol, which involved autotransfusion of shed blood. Measurement of actual hemoglobin loss in the Hammersmith series showed an eightfold reduction in the aprotinin-treated group.

Although overall mortality, myocardial infarction ratios, and indices of renal function were not significantly different in aprotinin or placebo groups, Dr Heric has mentioned a trend toward increased myocardial infarction rate and a trend toward renal dysfunction in the aprotinin group. These concerns are in contrast to current European and United Kingdom experience.

In a recent United Kingdom open study of 671 patients all receiving the high-dose aprotinin regimen, the incidence of side effects was low, specifically only 3 cases of renal failure, an incidence of 0.4%, and 1 case of coronary vein graft thrombosis, an incidence of 0.1%. Death due to myocardial infarction was reported in only 1.2% of patients. These discrepancies are intriguing and require further investigations.

Dr Heric, would you please comment, therefore, on, first, potential differences in the patient populations, second and most important, the anticoagulation regimen used in the Cleveland study, specifically the activated clotting time levels achieved and the total heparin doses in the aprotinin and placebo groups, and, third, the number of patients making up the six thrombosed vein grafts in the aprotinin group?

Finally, I would like to give an overview of our current thinking regarding aprotinin therapy based on the concept of the risk/benefit equation. The benefits of aprotinin therapy lie in its powerful effect on blood conservation and the potential reduction in the systemic inflammatory response to cardiopulmonary bypass. The risks, potential or actual, relate to a prothrombotic state and renal dysfunction, although the latter is, I believe, not a reality.

In addition, we are likely to be influenced by the risk category of the individual patient. Our perception of this risk/benefit equation will undoubtedly influence our use of this powerful drug.

I thank The Society for the opportunity to discuss this very interesting report.

DR HERIC: Thank you, Mr Taylor, for your comments. First, there are differences in the way that we handle chest tube drainage at The Cleveland Clinic compared with Dr Taylor's group, and I agree that we may have underestimated the efficacy of aprotinin by not measuring hemoglobin loss. We do not measure the differences in red cell mass lost. In that manner we probably underestimated actual reduction in shed blood.

It is difficult to account for the difference in findings compared with Dr Taylor's experience in a group of patients that included a wide variety of cardiac procedures. I think perhaps we do have a different patient population. Ten percent of our patients have had at least two previous coronary operations. The tenuous nature of the revascularized coronary circulation in such a reoperative group may place them at higher risk of graft thrombosis and may have led to our observed incidence of myocardial infarction.

We have speculated that because there is a dose-response increase in the activated clotting time in patients who receive aprotinin and thus a decreased heparin requirement on bypass, we may be under-anticoagulating our patients. We are interested in this. We have not addressed it rigorously yet. It would seem unlikely that this is the cause of graft thrombosis after separation from cardiopulmonary bypass.

Nine of our 13 postoperative deaths occurred in patients who had received aprotinin, either high-dose or low-dose. Five of 9 patients underwent autopsy, and all of their vein grafts were studied. We found 50% of these vein grafts to be occluded.

DR ERNST WOLNER (Vienna, Austria): We have performed at Vienna University a similar double-blind, randomized study in 120 patients using high-dose aprotinin, low-dose aprotinin, and placebo, and we found similar results concerning blood loss and blood transfusion requirements. However, we could not find similar results regarding postoperative myocardial infarction.

And this was supported by a reangiography study in 15 patients in each group that showed the patency rate in all three groups to be 93%.

We went back to the laboratory and made some investigations on isolated human endothelial cells, and we found that aprotinin decreased, in a dose-related fashion, the liberation from the cell of prostaglandin F_1 and increased the liberation of thromboxane; as you know, prostaglandin prevents the aggregation of thrombocytes, and thromboxane, as the von Willebrand factor, which we found also in this study, increases the aggregation of thrombocytes and perhaps also compromises microcirculation.

My question is, were the areas where you observed these Q-waves and these new myocardial infarctions in regions of the myocardium that were supplied by a bypass graft—this would speak more for an increased thrombosis of these grafts—or, what I suspect, were the Q-waves in the infarcts more in areas that were not revascularized, as the right coronary artery was completely blocked, which speaks more for our results in the sense of a compromised microcirculation, especially during the reperfusion phase and during ischemic cardiac arrest during the operation?

DR HERIC: Let me answer your last question first, Dr Wolner. We sent electrocardiograms of all the patients in the aprotinin study to an independent analyzer outside The Cleveland Clinic, and we did not identify the location of the myocardial infarctions in any given patient relative to the grafted region. Therefore, I cannot answer that question.

I can only account for your observed different infarction rates by presuming differences in patient selection. Our reoperative group may have had more borderline grafts supplying smaller coronaries with reduced run-off. This anatomic substrate combined with an altered coagulation state may have increased our myocardial infarction rate. In a group of patients undergoing primary myocardial revascularization or other procedures the graft status is not so tenuous.

DR DEVENDRA S. SAKSENA (Bombay, India): I just wanted to bring to your notice a different group of patients in whom we have used aprotinin. We have been using aprotinin since the work of the Dutch groups in 1988, and we have primarily used it in redo valve operations in patients with valve failures and reoperations. In this group of patients we have used aprotinin in 228 patients. An important thing is that most of these patients have been in liver failure and have been receiving anticoagulants (either warfarin or some other sort of anticoagulants), and most of them were undergoing emergency operations.

In our experience, aprotinin has been used in low doses; we have not used high doses because of economic factors. We have used an initial dose of 200,000 IU at the time of incision and another 200,000 IU in the bypass machine. We have been really impressed with the lack of blood loss, and we have been able to do most of these operations without any notable blood replacement. We have also used this in children with deep cyanotic disease who we thought would have a bleeding problem during or after operation.

My two areas of concern are the real doses that are required to achieve these results, because we have used the low doses, and also the renal function. As has been outlined in our experience, particularly in children with cyanotic disease, we found that renal function had deteriorated to a much greater extent.

I thank you once again and compliment the Cleveland group for a beautiful study.

MR BEN BIDSTRUP (London, England): Dr Heric, I enjoyed your study and certainly it confirms our experience in redo operations throughout Europe, this being the first study that has been done across the Atlantic. I would like to get a bit more information about your heparin management. One of the things that really concerns me is this apparent problem of postoperative thrombosis; it is certainly not our experience in several thousand cases. Our heparin management has always been to give a standard dose of 300 U/kg as an initial dose and then maintain the activated clotting time greater than 750 seconds. Would you comment on what your activated clotting times actually were and what your heparin management regimen was?

DR HERIC: Our standard regimen is to give the patients 300 U/kg of heparin before bypass and then to maintain the activated clotting time greater than 400 seconds and add heparin as required to maintain the activated clotting time greater than 400 seconds.

MR BIDSTRUP: This is a potential problem with the use of aprotinin. Because of, presumably, its effect on the intrinsic plotting cascade, it tends, independently of the effect of heparin, to increase the activated clotting time. I would support what you have said earlier and what Mr Taylor has said, that you might be under-anticoagulating these patients and perhaps placing them at risk for that very reason.

Aprotinin is not a heparin-sparing agent despite what has been suggested by others. One consequence of under-heparinization is intravascular coagulation.

Thank you for your attention.

DR HANS G. BORST (Hannover, Germany): I also greatly enjoyed the message from Cleveland, and I think this is very important in our day and age where at least in some quarters of the world aprotinin is being given in every open heart case; every adult heart case anyway. Thus we have administered the drug according to the high-dose regimen to 4,300 patients since July 1989. We have not noted any of these complications that you are alluding to, but admittedly we have not really looked for them specifically and may have to do that in the future.

However, I would like to draw your attention to two very severe complications we have had in readministering aprotinin in 2 of 48 redo operations that were done in patients who had received the drug during their primary operation. These patients had undergone aortic operation 2 and 5½ months previously and expected another aortic procedure. During induction of anesthesia, when they had received 750,000 and 250,000 U of the drug, respectively, they both went into severe hypotension and subsequently had their heart massaged for about a quarter of an hour. They received antihistaminics, calcium, arterenol, and cortisone, and within half an hour came out of this rather dangerous situation. The patients were reoperated on 10 days later, of course without aprotinin, and had an uneventful course.

I think this and the Cleveland experience demonstrate that the use of the drug probably should be individualized, noting its risk and benefits. My question, Dr Heric, is, have you identified patients who seem to be at a very special risk of the complications you described, and if so can you suggest any countermeasures, such as continuation of heparin administration or resumption of heparin early on?

DR HERIC: We have not been able to identify patients who are at especially high risk from aprotinin for thrombotic complications. We believe that aprotinin is a very powerful drug that has utility in decreasing bleeding and that we need to determine what patient is going to benefit most from aprotinin.

We have used aprotinin in patients other than reoperative coronary patients. One patient died after reoperative aortic root replacement for Marfan syndrome. At postmortem examination, multiple thrombi, both platelet and fibrin thrombi, were found throughout the circulation. Our cardiac pathologists inform us that this is a unique pathologic picture similar to that found in disseminated intravascular coagulation. This has increased our concern about aprotinin and what it may do to the coagulation system.

Mediastinitis in Heart Transplantation

Shreekanth V. Karwande, MD, Dale G. Renlund, MD, Stephanie L. Olsen, MD,
William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, John A. Hawkins, MD,
Roger C. Millar, MD, and John D. Marks, PE

Division of Cardiothoracic Surgery, University of Utah School of Medicine, and Utah Transplant Affiliated Hospitals Cardiac Transplant Program, Salt Lake City, Utah

Between March 1985 and December 1991, mediastinitis developed in 12 of 420 cardiac transplantation patients (2.8%). The mortality rate in this group of patients was 8.3% (1/12). Actuarial survival (1 year, 75%; and 5 years, 65%) was not significantly different from that of the group without mediastinitis (1 year, 88%; and 5 years, 75%). A higher percentage of the patients in the group with mediastinitis were listed as UNOS status 1 (50% versus 35%) and had a history of previous sternotomies (58% versus 44%). The presentation of mediastinitis was typical. Computed tomographic scanning with or without aspiration was a valuable adjunct in the diagnosis of mediastinitis. Induction immunotherapy with minimal steroids in the perioperative period was used in all patients. This may contribute to the patients' ability to mount an appropriate and effective response to infection, permitting earlier diagnosis. The debridement irrigation technique used in 8 of 12 patients had a low success rate of 33%, whereas the debridement muscle flap technique used in 4 of 12 was 100% successful in eliminating infection.

(Ann Thorac Surg 1992;54:1039–45)

In the face of the rapid and continued growth of heart transplantation, it is essential to continuously scrutinize the results and complications of this procedure. Mediastinitis is one of the most serious complications after heart operations. It carries a high mortality and significant morbidity. Additionally, heart transplant recipients represent a group of patients in whom decreased immune defenses present a unique situation. Transplant literature is surprisingly sparse with regard to mediastinitis. Most reports have involved few patients [1–3] or examined patients in the preinduction therapy era [4].

We retrospectively studied mediastinitis in 420 consecutive patients undergoing orthotopic heart transplantation from March 1985 to December 1991. The term *mediastinitis* defines a retrosternal infectious process with or without sternal instability. This definition does not include a superficial infection or a subcutaneous process confined to the anterior aspect of the sternum. Patients included in this review fit the criteria described above.

This study was designed to investigate several questions: (1) the incidence of mediastinitis in heart transplant patients and its attendant mortality and morbidity, (2) predisposing or risk factors, (3) clinical presentation, (4) diagnosis, and (5) surgical options.

Material and Methods

The Utah Transplant Affiliated Hospitals Cardiac Transplant Program is based in three hospitals in the Salt Lake City valley. The recipient criteria, immunosuppressive protocols, perioperative management protocols, and biopsy schedules were standardized. The operations were performed by surgeons at three different hospitals with comparable survival rates. The antibiotic regimen, skin preparation, and draping in the three hospitals were similar.

The technical details of the recipient operation and the donor harvest were standardized, as were the donor heart transport and packaging techniques. A crystalloid cardioplegic solution was used. The sternum was closed with interrupted stainless steel wires. The fascia and the subcutaneous and subcuticular tissues were closed with continuous absorbable sutures. All patients received prophylactic antibiotics. Cefuroxime was given at least ½ hour before the skin incision. Antibiotics were added to the pump prime and were administered for 48 hours postoperatively. Reverse isolation was not used.

Early rejection prophylaxis was based on equine antithymocyte globulin (polyclonal antibody) or murine monoclonal CD-3 antibody (OKT3). Our current immunosuppressive protocol involves a 14-day course of OKT3 beginning with a dose intraoperatively at the time of the pulmonary artery anastomosis. Intraoperative administration has the advantage of attenuating the first dose reaction and antigen recognition when the aortic cross-clamp is removed. OKT3 levels and CD3 lymphocyte counts are monitored daily for 14 days. Cyclosporine administration is begun on the third or fourth postoperative day at an oral dosage of 6 mg $\cdot$ kg^{-1} $\cdot$ day^{-1} and is adjusted to a target trough level of 150 to 200 mg/mL. Azathioprine (2 to 4 mg/kg) is administered preoperatively, and the postoperative dosage is adjusted to maintain the white blood cell count between 4 and 6 × 10^9/L (4,000 and 6,000/μL). Methylprednisone is administered intraoperatively (500 mg intravenously). Corticosteroids

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Karwande, Division of Cardiothoracic Surgery, University of Utah Medical Center, 50 North Medical Dr, Salt Lake City, UT 84132.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Characteristics of Patients[a]

Variable	Mediastinitis	No Mediastinitis
Number	12	408
Age (y)	52 ± 11	49 ± 13
Donor age (y)	29 ± 11	27 ± 11
Male (%)	100	82
Preoperative Diagnosis (%)		
IDC	8	34
CAD	75	55
Other	17	11
UNOS status 1 (%)	50	36
Transplant wait (d)	88 ± 107	54 ± 60
Ischemic time (min)	167 ± 45	172 ± 62
Redo operation (%)	58	42
EF	0.18 ± 0.09	0.18 ± 0.08
CI ($L \cdot min^{-1} \cdot m^{-2}$)	2.0 ± 0.5	2.0 ± 0.6
IABP/VAD	1 (8%)	43 (12%)

[a] Values are reported as discrete, percentage, or mean ± standard deviation.

CAD = coronary artery disease; CI = cardiac index; EF = ejection fraction; IABP = intraaortic balloon pump; IDC = idiopathic dilated cardiomyopathy; UNOS = United Network for Organ Sharing; VAD = ventricular assist device.

(prednisone or equivalent) are then administered at 0.25 $mg \cdot kg^{-1} \cdot day^{-1}$ until the completion of the OKT3 course, when the dosage is increased to 1 $mg \cdot kg^{-1} \cdot day^{-1}$ for 7 days. A steroid taper is begun immediately and discontinued in the following 2 weeks; it is only reinstituted for episodes of rejection. Surveillance biopsies are performed as per standard protocol. Management of rejection episodes has been described in detail elsewhere [5].

Transplant patients were grouped by presence or absence of mediastinitis. Statistical differences between groups were analyzed using the χ^2 or Fisher's exact test, as appropriate, for discrete variables, and unpaired Student's t tests for continuous variables. Odds ratios for risk factors were calculated from contingency tables and are reported with 95% confidence intervals. Multivariate analysis of risk factors was performed using a logistic stepwise regression model. Actuarial survival was determined by the Kaplan-Meier method, with significance of comparisons determined by the Tarone-Ware test. Statistical significance was considered for an α level of 0.05 ($p < 0.05$).

Results

A total of 12 mediastinal infections occurred in 420 patients for an overall incidence of 2.8%. One of these patients died, yielding a mortality rate of 8.3% (1/12). There were three late deaths, which were unrelated to mediastinitis. Demographic and descriptive characteristics of transplant patients with and without mediastinitis are shown in Table 1.

The following risk factors were analyzed for inclusion in a step-wise logistical regression model for prediction of mediastinitis: age, sex, time on wait list, ejection fraction, pulmonary capillary wedge pressure, cardiac index, circulatory support, United Network for Organ Sharing (UNOS) status, donor heart ischemic time, cross match, cause of cardiac disease, previous sternotomy, year of transplantation, and immunosuppressive protocol. Risk factors identified in the model (criterion, $p < 0.15$) included year of transplantation, cause of cardiac disease, and UNOS status. Higher risk was associated with transplantation in earlier years, coronary artery disease as the cause of cardiac disease, and a pretransplantation UNOS status of 1. Knowledge of cause significantly improved the model ($p = 0.03$).

Differences were observed in terms of preoperative diagnosis and severity of illness before operation. Mediastinitis was 2.7 times (95% confidence interval 0.71–10.8) more likely to develop in patients listed for transplantation for ischemic cardiomyopathy than in other transplant patients. Seven of the 12 patients in whom mediastinitis developed had had prior sternotomy (58%). This is higher than the general transplant population, in which repeat operations comprise only 44% of the patients. Mediastinitis was 1.9 times (95% confidence interval, 0.56–6.03) more likely to develop in patients with one or more prior sternotomies. Six of the 12 recipients with mediastinitis (50%) had UNOS status 1 before their transplantation. These patients were in the intensive care unit for varying lengths of time receiving intravenous inotropes before transplantation. In comparison, pretransplantation inotropic support was required in 36% of the general transplant population. Mediastinitis was 1.9 times (95% confidence interval, 0.56–6.48) more likely to develop in patients listed as UNOS status 1 than in other transplant patients.

One patient had an intraaortic balloon pump in place. Although it is customary for central lines to be inserted before transplantation in all patients, 6 of the 12 patients in whom mediastinitis developed had central line placement or Swan-Ganz monitoring performed for hemodynamic reasons. The average pretransplantation wait was 88 days and did not differ from the general transplant population. The average cross-clamp time was 81 minutes. The ischemic time was 167 minutes and the pump time was 122 minutes. These figures are not statistically different from those of the patients without mediastinitis. All patients were extubated within 24 hours.

Blood loss and blood product requirements were reviewed. These were not found to be excessive. The average total chest tube drainage was 741 mL. All patients received fresh-frozen plasma preoperatively because all had been placed on full oral anticoagulation, which needed to be reversed at the time of transplantation. One of the 12 patients in whom mediastinitis developed (8%) was reexplored for mediastinal bleeding.

The postoperative course of these patients after the development of mediastinitis was complicated. Four of the 12 patients required a variety of procedures to be performed (colonoscopy, suture ligation of bleeding duodenal ulcer, femoral embolectomy). Dialysis was required in 2 of 12 patients (17%). Postoperative opportunistic pneumonias were seen in 4 of 12 patients (enterococcus,

Table 2. Surgical Technique

Procedure	No. of Patients	Success	Complications
Debridement and irrigation	8/12 (66%)	3/8 (37%)	Bleeding (1), seroma (2)
Debridement and muscle flaps	4/12 (34%)	4/4 (100%)	None

Legionella, and cytomegalovirus). Two of 12 patients (16%) had recognizable sepsis before transplantation and had been treated with appropriate antibiotics with resolution.

The presentation of mediastinitis was quite typical. The usual presenting signs and symptoms were elevated white blood cell count (100%), pain (66%), fever (66%), drainage, sternal instability, and shock (25%). The most common were fever and pain. Pain, seen in 8 of 12 patients (66%), was out of proportion with physical findings and often preceded other manifestations. Drainage, sternal instability, and fluctuance were less common. The average time of presentation was 9 days after operation, with a range of 5 to 17 days. Shock was the first presentation of mediastinitis in 3 patients. Two of these 3 required tracheal intubation and inotropic support. In spite of immunosuppression with azathioprine, all patients presented with an elevated white blood cell count, which ranged from 11 to 35 × 10^9/L (11,000 to 35,000/μL). *Staphylococcus* species was cultured from the majority of these wounds (11/12). There was one *Legionella* infection. No polymicrobial infections were seen. There was no relationship between the type of organism and outcome.

Debridement, sternal closure, and irrigation was the most commonly used initial surgical procedure (8/12; 66%) (Table 2). This procedure, however, was unsuccessful in eliminating the infection in 5 of these patients (62%). All 5 eventually required muscle flaps to effect healing. The single death of this series was in this group. Debridement and muscle flap closure as a two-stage procedure was used as the initial surgical management in 4 of 12 patients (34%) with no failures and no mortality. The choice of the initial surgical procedure was based on surgeon preference. Debridement and muscle flap closure as a single-stage procedure was not used in this series.

There were no significant differences in actuarial survival between patients with mediastinitis (75% at 1 year and 64% at 5 years) and the general transplant population (88% at 1 year and 75% at 5 years; $p = 0.70$).

Morbidity and mortality after hospital discharge are significant in the nontransplant cardiac surgical population with mediastinitis. Survival of 86% at hospital discharge fell to 75% in 3 years in one series [6]. In this series of transplant patients discharged from the hospital after recovery from mediastinitis, the survival rate is similar to that of other transplant patients (Fig 1).

Comment

Surgical Technique

Deep infections of sternotomy wounds occur with a reported incidence of 0.3% to 5% in the general cardiac surgical population. Our incidence of sternal wound infection in the nontransplant population is less than 1%. In the transplant population this incidence is more than doubled at 2.8%. The pathogenesis of sternal infections is still unclear. Grossi and associates [7] postulate a localized area of osteomyelitis within the sternal marrow without external signs except for localized pain, a situation similar to an abscess in a bone in other locations. Such a localized area of osteomyelitis is not well penetrated by systemic antibiotics, and unless drained the infection spreads to adjacent costal cartilage and underlying mediastinum. Others believe that instability of sternal fragments is the cause of most sternal infections.

Prolonged antibiotic treatment of mediastinitis as reported by Serry and colleagues [8] carries an unacceptable morbidity and mortality and has been abandoned. Sternal

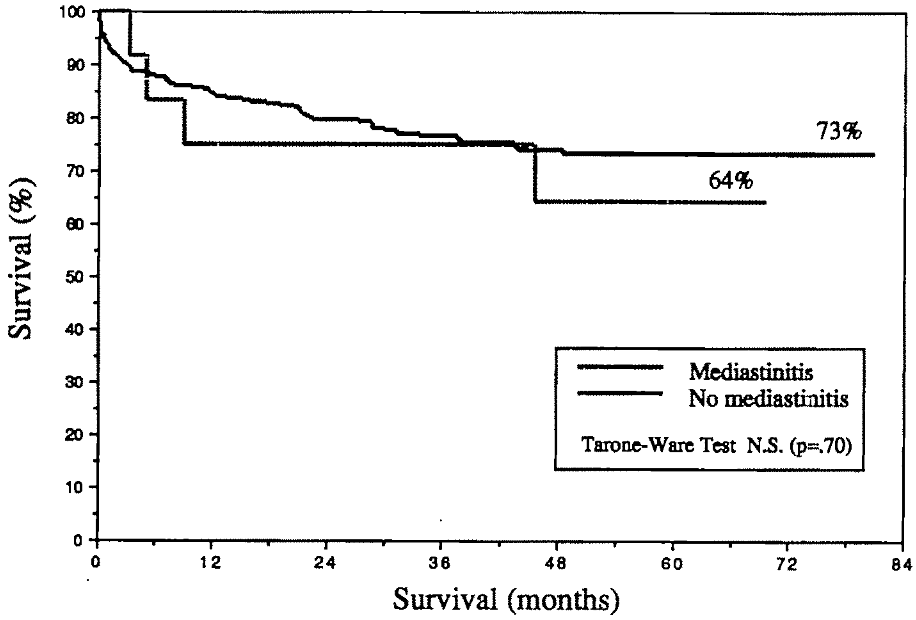


Fig 1. Actuarial survival analysis of patients with and without mediastinitis. Statistically the difference was not significant (N.S.).

debridement, dressing changes, and closure by secondary intention with a mortality of about 30% [7] was the most widely used treatment until 1963. At that time, Shumacker and Mandelbaum [9] described a technique of closed catheter irrigation of the mediastinum after debridement and closure of the sternum. This technique was further modified in 1968 by Bryant and associates [10]. Dilute antimicrobial solution was irrigated through the mediastinum until the wound infection clinically resolved or until cultures of the effluent were negative. The mortality of poststernotomy mediastinitis using this technique was reduced to 20%. Thurer and associates [11] described the use of 0.5% povidone-iodine (Betadine) solution as a mediastinal irrigant and reported it to be an effective antimicrobial and nontoxic in the concentrations used. Since then, however, iodine toxicity has been reported and the use of this irrigant solution has been abandoned in some centers [12].

Lee and colleagues [13] in 1976 offered the first alternative to open granulation in those patients whose infection was not resolved by catheter irrigation. After wide debridement, omentum was transposed into the mediastinum. Jurkiewicz and co-workers [14] expanded on this concept and advocated the use of muscle flaps instead of omentum. Their report led to a dramatic increase in the use of muscle flaps and was accompanied by impressive results from different centers. Procedure mortality was largely eliminated and success rates climbed to more than 90%.

The original technique [14] called for an interval period of open packing to prepare the mediastinal bed before swinging muscle flaps. Recently, however, a number of centers have reported a single-stage procedure involving debridement and muscle flap mobilization without compromising success [15, 16].

Based on this experience a number of principles have evolved in the surgical management of mediastinal infections [17]: (1) Early recognition is crucial. (2) Adequate debridement and removal of all foreign bodies and devascularized bone is essential. (3) Obliteration of all mediastinal dead space with vascularized muscle flaps is preferred.

Simple debridement and irrigation has been recommended in patients whose mediastinal structures are soft and pliable as opposed to those who have a thick fibrous peel that prevents obliteration of the mediastinal space [17]. In the transplant patient, however, the mediastinum is usually wide due to chronic cardiac dilatation, and suction obliteration of mediastinal space may be inadequate even if these tissues are pliable. Our own data reflect a high failure rate (66%) of the debridement-irrigation technique.

Muscle flaps most commonly used include one or both pectoralis major muscles and unilateral rectus abdominis muscle. The pectoralis may be based on the thoracoacromial or intercostal branches of the internal mammary artery. The rectus abdominis is based on the superior epigastric artery. Flap mobilization techniques have improved to reduce blood loss, decrease seroma formation, and maintain form and function [15, 18]. Although respiratory mechanics are always a concern, none of our patients had prolonged respiratory problems related to the sternal debridement and flaps. Other reports in the literature tend to support this observation [15, 19]. Muscle flap treatment simplifies nursing care, helps ambulation, avoids psychological stress, and simplifies immunosuppressive management in the event of a rejection episode. We currently favor the muscle flap technique in the management of these infections.

Presentation and Diagnosis

In all cases reviewed, presentation of mediastinitis was fairly typical with an elevated white blood cell count, pain, and fever. These signs and symptoms appeared during the initial hospitalization. We believe that induction immunotherapy and a low dose of steroid therapy in the first 14 days enable the recipient to mount an appropriate clinical response to the infection. This is in contrast to the report by Trento and associates [4] on 6 patients with mediastinitis after transplantation, in which the use of triple-drug therapy masked signs and symptoms, resulting in frequent late diagnosis.

In our series the diagnosis was fairly simple because of classic symptoms. Additionally, computed tomographic scanning of the mediastinum proved to be an extremely useful diagnostic tool. Coupled with aspiration, the accuracy of computed tomographic scanning for diagnosis of mediastinitis was 100%. There was one false-negative computed tomographic scan performed without aspiration in a patient with mediastinitis. Computed tomographic scanning also was useful in postoperative surveillance after surgical treatment of mediastinitis. The accuracy of computed tomographic scanning in this setting even without aspiration is 100%.

Immunosuppression

Cardiac transplantation has evolved from a heroic sporadically successful clinical experiment in the late 1960s to a widely accepted therapeutic modality with a high degree of success. In the early years of cardiac transplantation, only nonselective immunosuppression with corticosteroids and antimetabolites such as azathioprine, cyclophosphamide, or actinomycin D was available. Rejection frequency and infection rates were high.

The introduction of cyclosporine-based immunosuppression in the early 1980s led to dramatic increases in survival and quality of life [5]. Because of the selectivity of cyclosporine, rejection was more often a chronic smoldering process rather than an acute fulminant event. Triple therapy (cyclosporine, azathioprine, and corticosteroids) was rapidly adopted and became the standard immunosuppressive regimen used in cardiac transplantation. This in turn led to liberalization of recipient and donor criteria and a proliferation of centers offering cardiac transplantation. In recent years, therefore, patients with certain systemic diseases or end-organ dysfunction are being considered for cardiac transplantation.

Immunosuppression in these patients has to be carefully regulated. The object is to develop a therapeutic window, wherein the degree of immunosuppression is sufficient to prevent allograft rejection but leaves the host sufficiently immunocompetent with regard to pathogenic

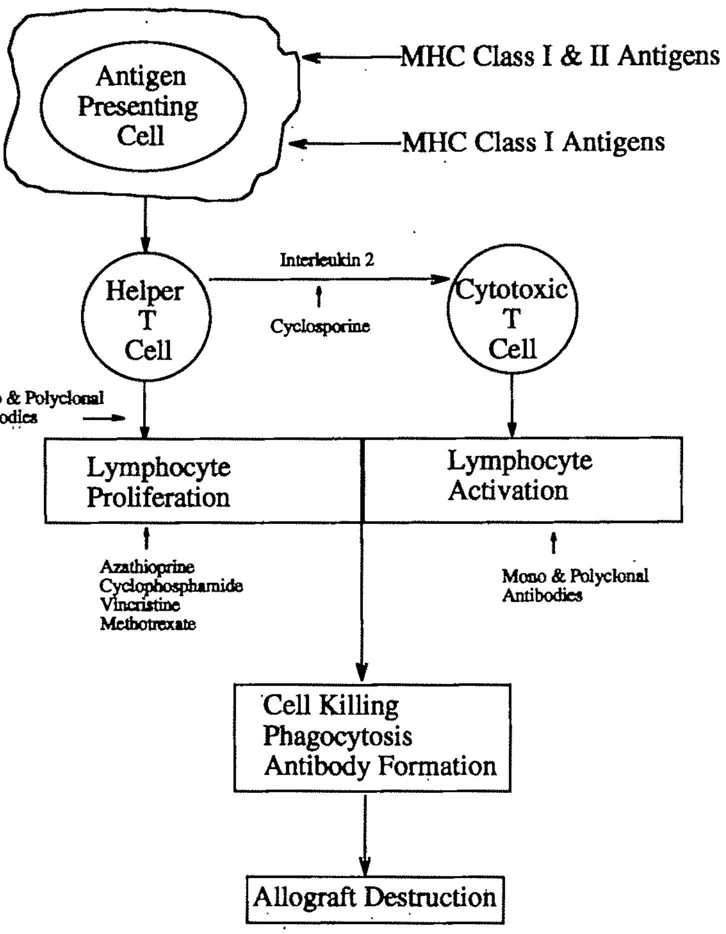


Fig 2. Cascade of events leading to allograft destruction. Allograft rejection occurs when foreign antigen is processed by antigen-presenting cells and presented to mature helper or cytotoxic T lymphocytes. Processed antigen presented to helper T lymphocytes induces the formation of cytotoxic T lymphocytes by the synthesis and secretion of interleukin 2. Once mature T lymphocytes have recognized foreign antigen, lymphocyte proliferation occurs, leading to cell killing, phagocytosis, and antibody formation. Left unchecked, allograft destruction ultimately occurs.

organisms or neoplastic processes. Our goal is to selectively and potently block the cascade of events leading to allograft destruction (Fig 2) with a combination of older and newer immunosuppressive agents. Table 3 lists future immunosuppressive agents and their mechanisms of action. Increased selectivity is the goal of future immunosuppressive protocols.

It is generally established that greater immunosuppression is required earlier after organ transplantation rather than later. This lesser requirement with time is believed to develop as a result of the gradual emergence of suppressor mechanisms [20]. Aggressive early prophylaxis using cytolytic therapy delays the first episode of allograft rejection until the allograft has recovered from the ischemic insult and the surgical wounds have healed [21]. Whether early cytolytic therapy will enhance or hasten development of allograft tolerance is an unresolved issue.

Nevertheless, routine administration of potent antilymphocyte preparations for early prophylaxis is used by almost 50% of the transplant centers [22]. This is in the hope of inducing the host to be more tolerant to the allograft, so-called "induction therapy." Yacoub and associates in 1985 first suggested the use of early cytolytic therapy (polyclonal) leading to steroid withdrawal. When OKT3 became available for clinical trials, prophylactic administration in cardiac transplantation was pursued because of its predictable potency, easy availability, and lack of contamination with blood products.

Table 3. Future Immunosuppressive Agents

Agent	Mechanism of Action
FK-506	Interferes with the production of interleukin 2 from helper T lymphocytes, blocking the induction of cytotoxic T lymphocytes
RS-61443	Blocks the only pathyway, the de novo pathway, in lymphocytes for purine biosynthesis
Rapamycin	Suppresses interleukin 2 and interleukin 4-driven lymphocyte proliferation
Anti-pan T lymphocyte antibody-Ricin A chain immunoconjugate monoclonal antibody	Blocks protein synthesis in CD-5 positive lymphocytes by enzymatically cleaving a specific adenosine linkage in ribosomal RNA
OKT4a	Selectively reacts with and depletes CD-4 positive lymphocytes, suppressing the generation of primary cytotoxic responses
Anti-interleukin 2 receptor monoclonal antibody	Inhibits functional interleukin 2 to interleukin 2-receptor interaction

OKT3 is a murine anti-CD3 monoclonal antibody. It was initially used to treat allograft rejection refractory to corticosteroids and polyclonal antilymphocytic preparations [23]. OKT3 was introduced into early rejection prophylaxis protocols in the hope of delaying rejection and to block antigen recognition. This in turn would result in fewer rejection episodes.

With this background, induction therapy was adopted by the Utah Transplant Affiliated Hospitals Cardiac Transplant Program with the following goals in mind: (1) Delay the first rejection episode. (2) Decrease the severity and frequency of rejection episodes. (3) Establish a relatively drug free and rejection free interval immediately postoperatively to allow for wound healing.

Our own experience seems to support these objectives [21]. Data from other centers with respect to efficacy of OKT3 are quite varied [24–26]. The large discrepancy in comparative efficacy is in part explained by differences in the immunosuppressive protocols independent of OKT3 administration. Recently, Prieto and co-workers [27] and Reid and associates [6] have reported their experience with high-risk patients managed by induction immunotherapy. They found that these patients required smaller doses of immunosuppressive drugs in the early postoperative period and had fewer serious infections without compromising long-term survival.

Clearly, in high-risk patients immunosuppression needs to be individualized to reduce the risk of infection and assure allograft survival. With several new and potent immunosuppressive agents on the horizon (see Table 3), the hope that selective immunosuppression for high-risk patients will improve in the years to come is realistic.

Conclusions

Mediastinitis after cardiac transplantation is twice as likely to occur compared with nontransplant cardiac operations. The major risk factor predisposing to mediastinitis is the patient's preoperative condition. Patients in the intensive care unit on intravenous inotropic support, those who are listed in UNOS status 1, and those having had previous sternotomies have a higher risk for development of mediastinitis. Elevation of the white blood cell count, incisional pain out of proportion with physical findings, or unexplained shock in the first few weeks after transplantation should be construed as mediastinitis unless proved otherwise. Computed tomographic scanning with aspiration is a valuable adjunct in the diagnosis of mediastinitis, and its liberal use is recommended. Because of the high failure rate of the debridement-irrigation technique, a single- or two-stage application of the debridement-muscle flap technique is our current choice. Induction immunotherapy and avoidance of high-dose steroids in the perioperative period may allow the patient to mount an appropriate and effective response to infection, either preventing mediastinitis or allowing it to be diagnosed earlier.

References

1. Frimpong-Boakeng K, Warnecke H, Schuler S, Haverich A, Borst HG. Transposition of the greater omentum for management of mediastinal infection following orthotopic heart transplantation: a case report. J Heart Transplant 1986;5:330–1.
2. Miller R, Ruder J, Karwande SV, Burton NA. Treatment of mediastinitis after heart transplantation. J Heart Transplant 1986;55:477–9.
3. Pearl SN, Weiner MA, Dibbel DG. Sternal infection after cardiac transplantation. Successful salvage utilizing a variety of techniques. J Thorac Cardiovasc Surg 1982;83:632–4.
4. Trento A, Dummer GS, Hardesty RL, Bahnson HT, Griffith BP. Mediastinitis following heart transplantation: incidence, treatment and results. Heart Transplant 1984;4:336–40.
5. Renlund DG, O'Connell JB, Bristow MR. Strategies of immunosuppression in cardiac transplantation. Semin Thorac Cardiovasc Surg 1990;2:181–8.
6. Reid KR, Menkis AH, Novick RJ, et al. Reduced incidence of severe infection after heart transplantation with low-intensity immunosuppression. J Heart Lung Transplant 1991; 10:894–900.
7. Grossi EA, Culliford AT, Krieger KH. A survey of 77 major infectious complications of median sternotomy: a review of 7949 consecutive operative procedures. Ann Thorac Surg 1985;40:214–23.
8. Serry C, Bleck PC, Javid H, et al. Sternal wound complications: management and results. J Thorac Cardiovasc Surg 1980;80:861–7.
9. Shumacker HB Jr, Mandelbaum I. Continuous antibiotic irrigation in the treatment of infection. Arch Surg 1963;86: 384–7.
10. Bryant LR, Spencer FC, Trinkle JK. Treatment of median sternotomy infection by mediastinal irrigation with an antibiotic solution. Ann Surg 1969;169:914–20.
11. Thurer RJ, Bognolo D, Vargas A, Isch JH, Kaiser GA. The management of mediastinal infection following cardiac surgery. An experience utilizing continuous irrigation with povidone iodine. J Thorac Cardiovasc Surg 1974;68:962–8.
12. Glick PL, Guglielmo BJ, Tranbaugh RF, Turley K. Iodine toxicity in a patient treated by continuous povidone-iodine mediastinal irrigation. Ann Thorac Surg 1985;39:478–80.
13. Lee AB Jr, Schimert G, Shatkin S. Total incision of the sternum and thoracic pedicle transposition of the greater omentum: useful strategems in managing severe mediastinal infection following open heart surgery. Surgery 1976;80: 433–6.
14. Jurkiewicz MJ, Bostwick J III, Hester TR, Bishop JB, Craver J. Infected median sternotomy wound. Successful treatment by muscle flaps. Ann Surg 1980;191:738–43.
15. Jeevanandam V, Smith CR, Rose EA, Malm JR, Hugo NE. Single stage management of sternal wound infections. J Thorac Cardiovasc Surg 1990;99:256–63.
16. Nahai F, Rand RP, Hester TR, Bostwick J, Jurkiewicz MJ. Primary treatment of the infected sternotomy wound with muscle flaps. A review of 211 consecutive cases. Plast Reconstr Surg 1989;84:434–41.
17. Pairolero PC, Arnold PC. Management of infected median sternotomy wounds. Ann Thorac Surg 1986;42:1–2.
18. Nahai F, Morales L Jr, Bone DK, Bostwick J III. Pectoralis major muscle turnover flaps for closure of the infected sternotomy wound with preservation of form and function. Plast Reconstr Surg 1982;70:471–4.
19. Neale HW, Kreilein JG, Schreiber JT, Gregory RO. Complete sternotomy for chronic myelitis with reconstruction using a rectus abdominis myocutaneous island flap. Ann Plast Surg 1981;6:305–14.
20. Lafferty KJ, Prowse SJ, Simeonlvic CJ. Immunobiology of tissue transplantation: a return of the passenger leukocytic concept. Annu Rev Immunol 1983;1:143–73.
21. Renlund DG, O'Connell JB, Gilbert EM, et al. A prospective comparison of murine monoclonal CD-3 (OKT3) antibody-based and equine antithymocyte globulin-based rejection prophylaxis in cardiac transplantation. Decreased rejection and less corticosteroid use with OKT3. Transplantation 1989; 47:599–605.
22. A report of the working group of transplant cardiologists. Efficacy of induction and non-induction immunosuppression in cardiac transplantation [Abstract]. J Heart Transplant 1990;9:61.
23. Gilbert EM, DeWitt CW, Eisworth CE, et al. Treatment of refractory cardiac allograft rejection with OKT3 monoclonal antibody. Am J Med 1987;82:202–6.

24. Constanzo-Nordin MR, O'Sullivan EJ, Johnson MR, et al. Prospective randomized trial of OKT3 versus horse antithymocyte globulin-based immunosuppressive prophylaxis in heart transplantation. J Heart Transplant 1990;9:306–15.
25. Kirklin JK, Boulge RC, White-Williams C, et al. Prophylactic therapy for rejection after cardiac transplantation. J Thorac Cardiovasc Surg 1990;99:716–24.
26. Frist WH, Merrill WH, Eastburn TE, et al. Unique antithymocyte serum versus OKT3 for induction immunotherapy after heart transplantation. J Heart Transplant 1990;9:489–94.
27. Prieto M, Lake KD, Pritzker MR, et al. OKT3 induction and steroid-free maintenance immunosuppression for treatment of high risk heart transplant recipients. J Heart Lung Transplant 1991;10:901–11.

DISCUSSION

DR THOMAS M. EGAN (Chapel Hill, NC): I would like to congratulate you for your success, and I had a question about your recommendation for muscle flaps as a primary procedure to deal with this very difficult problem. If 3 of 8 patients can be spared muscle flaps and then the balance subsequently salvaged, why do you propose not going to the less aggressive procedure first? In your abstract you suggested that the death was related to acute rejection and not to failure of your muscle flaps.

DR KARWANDE: Well, first we have had a high failure rate with the debridement-irrigation technique. Muscle flap coverage makes the management of these patients after the surgical therapy simpler, ie, when rejection develops I think the treatment of rejection is simplified. You are not concerned about using steroids on these patients because you feel secure in the fact that their dead space has been obliterated with a viable muscle flap.

The second reason is that patients who tend to fail debridement and irrigation, and their percentage is high in our series, have a prolonged hospital stay. The only fatal outcome we had was in a patient who had failed the debridement-irrigation technique; I believe we lost the window of opportunity and the subsequent cascade of events led to his death.

DR RICHARD J. NOVICK (London, Ont, Canada): We have performed 294 heart transplantations and have had 10 cases of mediastinitis. All were treated with debridement, sternal reclosure, and mediastinal irrigation for 10 to 14 days, and none had recurrent infection. I therefore believe that the conclusion that the primary mode of therapy should be a muscle flap is not correct. What were the reasons for failure of the sternal closure technique? Was there infection with methicillin-resistant *Staphylococcus aureus*? Was there any residual sternal instability? What factors could you identify to indicate why those 4 or 5 patients failed?

DR KARWANDE: I think the main reason why those 5 patients failed the debridement-irrigation technique was because the dead space was not obliterated by the suction technique. Some of these patients have a stiff, nonpliable mediastinum, and in spite of chest tube suction the mediastinum is not obliterated. Many of these patients, as you very well know, have large pericardial cavities, and these cavities are, generally speaking, occupied by a small donor heart. I presume that one of the reasons why the debridement-irrigation technique failed was because the cavity was not obliterated.

DR HANS G. BORST (Hannover, Germany): I thoroughly enjoyed your presentation because we are both in agreement on certain points and in disagreement on others. We certainly agree with you, and I think you have proved it, that mediastinitis is not as catastrophic an event in transplant patients as one would suppose on account of the fact that the patient is immunocompromised.

We have had 6 such complications in a group about the size of yours for an incidence of mediastinitis of about 1.5%; however, all 6 patients had an unstable sternum, and in fact we have never seen the discrete type of mediastinitis that you are describing. All 6 patients had omental pull-up and all of them healed per primam. There was no need of applying any more advanced plastic procedures.

In addition, and more interestingly, we had 1 patient of 25 undergoing heart-lung transplantation who, on the 11th postoperative day, suddenly exsanguinated and was taken to the operating room where she was bleeding from the aortic cannulation site. During cardiac massage and mass transfusion, my co-worker, Dr Haverich, fixed the hole in the aorta and again did an omental pull-up, and this again resulted in primary healing. Lo and behold the causative agent was *Candida*!

So I think we fully agree with you that one should be aggressive about these cases of mediastinitis with the aim of completely filling up the retrosternal space, and I think these patients should be treated promptly before any extensive osteomyelitis develops, because then you will wind up with all kinds of plastic procedures trying to fill holes. But it nevertheless is very interesting that you have these discrete forms that we have never seen.

Now, if you do your plastic operations, do you add an irrigation system or do you just leave it like it is?

DR KARWANDE: I would like to compliment you on your low mediastinitis rate. I think what we are saying is basically the same thing. Instead of using omentum we have been using muscle. There is no irrigation involved when you use the pectoralis major muscle. You basically obliterate the dead space in the mediastinum using the muscle and then close the skin on top of it.

DR BORST: Don't you wind up with a big defect in the sternum then because you have to slip in the muscle somehow?

DR KARWANDE: The sternum is left open. Fortunately we have not seen problems related to this, by way of respiratory embarrassment or cosmetic deformity.

DR BORST: Oh, I see; the sternum was always closed in our patients.

DR EDWARD A. PASCOE (Winnipeg, Man, Canada): Coronary disease as the pretransplantation diagnosis I think also was an increased predictor of mediastinitis. Had many of those patients undergone myocardial revascularization with harvesting of internal mammary arteries, which might have made their chest walls relatively ischemic and more prone to infection?

DR KARWANDE: That is a very good question. We looked at that specifically, and we found only 2 patients of 12 in whom mediastinitis developed had internal mammary artery revascularization, and of the 12 patients in whom mediastinitis developed, we could detect an unstable sternum in only 3 patients.

Long-Term Effect of Total Fundoplication on the Myotomized Esophagus

Philippe Topart, MD, Claude Deschamps, MD, Raymond Taillefer, MD, and André Duranceau, MD

Division of Thoracic Surgery, Department of Surgery, Université de Montréal, Hôtel-Dieu de Montréal, Montreal, Quebec, Canada

From 1978 to 1983, 17 patients had an esophagocardiomyotomy with an added short total fundoplication as an antireflux procedure. Thirteen had achalasia and 4, diffuse esophageal spasm. All patients initially had the usual symptoms of these motor disorders. Early after the operation all became asymptomatic, but over the years of follow-up, symptoms reappeared in 14 of 17 patients, and 5 required reoperation. The distal esophageal transverse diameter showed progressive dilatation from 3.9 cm preoperatively to more than 6 cm after 10 years of evolution. Over the same period, deterioration in the esophageal emptying capacity caused esophageal stasis to increase from 32% to 75%. Manometric changes were significant after the operation: resting pressures in the esophageal body decreased from 10.5 to 4.4 mm Hg ($p <$ 0.001) proximally and from 12.2 to 4.6 mm Hg distally ($p < 0.001$). Peak contraction pressures became significantly weaker: 38 to 30 mm Hg in the proximal esophagus ($p <$ 0.001) and from 49.2 to 28.1 in the distal esophagus ($p <$ 0.001). Tertiary contractions were unchanged distally, but peristalsis reappeared in more than 30% of all swallows in the proximal half of the esophageal body. The resting pressure gradient in the lower esophageal sphincter area was reduced from 25.5 to 7.4 mm Hg by the operation. This gradient remained stable over 10 years of follow-up. No significant acid exposure was documented in 8 patients undergoing 24-hour pH recordings after their operation. Endoscopy revealed dilatation and retention without evidence of reflux esophagitis damage. Total fundoplication when associated with esophageal myotomy results in improved symptoms in the early postoperative phase. Aperistalsis remains unchanged, and the lower esophageal sphincter gradient remains low. Over time a progressive increase in esophageal retention occurs with poor emptying and recurrence of symptoms. Despite good reflux control, total fundoplication is not appropriate to the myotomized esophagus over time.

(Ann Thorac Surg 1992;54:1046–52)

Esophageal myotomy is the most valuable surgical palliation offered to patients with achalasia or diffuse esophageal spasm. It is still controversial to add an antireflux procedure at the distal end of the myotomized esophagus. When performing an esophageal myotomy for these primary motor disorders, surgeons have to face a reported reflux incidence of 3% to 52% when the lower esophageal sphincter gradient is reduced significantly [1]. Reflux control without compromising the emptying function of the disabled esophagus thus becomes an important goal of the surgical management of these conditions. A wide variety of antireflux operations have been proposed over the years. Most authors advise some type of fundoplication. This report aims at documenting the long-term effects of a 360-degree short fundic wrap as an added procedure immediately after myotomy.

Material and Methods

Clinical

From 1978 to 1983, 17 patients (9 men, 8 women) were assessed in the esophageal motility laboratory of our surgical division. They were aged 19 to 68 years (mean age, 42.1 years). The clinical presentation, a standard esophagogram, and esophageal emptying scintiscans, as well as manometry and endoscopy, were obtained in all 17 patients preoperatively. After the operation all 17 patients were reassessed using the same methods, with the addition of 24-hour pH recording when it became available. Results were analyzed at periods of 0 to 24, 25 to 48, 49 to 72, and 120 months postoperatively. The range of the esophageal work-up period was from 9 to 152 months after the operation (mean, 69 months).

Radiology

Standard esophagograms were obtained under fluoroscopic control with 6 printed frames per second. Measurement of the largest transverse diameter in the distal esophagus was obtained. Presence of abnormal contractions and quality of esophageal transit were assessed.

Esophageal Radionuclide Transit Study

The examination was performed using a single bolus of 0.1 mCi of technetium 99m diluted in 10 mL of water.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Duranceau, Department of Surgery, Hôtel-Dieu de Montreal, 3840, St-Urbain, Montreal, Que, Canada H2W 1T8.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Clinical Presentation[a]

Symptom	Preop	0–24 mo	25–48 mo	49–72 mo	73–120 mo
Regurgitation	7	3 (17)	4 (25)	5 (35)	6 (50)
Substernal pain	4	. . .	1	. . .	2
Aspiration	3	. . .	. . .	. . .	. . .
Slow emptying	. . .	1 } (12)	2 } (25)	1 } (21)	3 } (41)
Dysphagia	17	1	2	2	2
Odynophagia	2	. . .	. . .	. . .	. . .
Total	17/17 (100)	5/17 (29)	7/16 (43)	6/14 (42)	9/12 (75)

[a] Numbers in parentheses are percentages.

Data were acquired during a 3-minute period over each of three esophageal segments (upper, middle, and lower). The radioactivity retained in the esophagus was computed at 2 minutes and used as an objective measurement of the esophageal emptying capacity.

Manometry

A triple-lumen polyvinyl catheter (USCI Rinaldo Tube), each lumen having an internal diameter of 2.03 mm, was used for esophageal motility recordings between 1978 and 1983. Each lumen ended with 1.2-cm lateral openings spaced 5 cm apart and radially oriented at 120 degrees. The tube was introduced through the patient's nose and connected to external pressure transducers (Hewlett Packard 1280). Pressures were recorded in a four-channel physiograph (Hewlett Packard 7754 A) through Hewlett Packard 8805 C preamplifiers. A Harvard mechanical infusion pump perfused each lumen at a rate of 3.8 mL/min for the esophageal body and for the lower esophageal sphincter area. Ten wet swallows of 2 mL of water were given to the patient while pressures were recorded in each of three specific esophageal zones: the proximal half of the esophagus, the distal half of the esophagus, and the lower esophageal sphincter (LES) area. All pressures were computed in millimeters of mercury with the 0 reference point being atmospheric pressure. Assessment of the LES was performed using a station pull-through technique in the sphincter area.

24-Hour pH Recording

To document reflux events a Sandhill (Littleton, CO) ambulatory pH recorder was used. After calibration the antimony electrode was placed 5 cm above the gastroesophageal junction previously identified and localized by manometric recording. The 24-hour recording was always obtained in an ambulatory fashion. Results were computed in total episodes and total minutes of reflux, reflux episodes of more than 5 minutes, the longest reflux episode, and the total percent exposure to acid.

Endoscopy

The endoscopic assessment of the esophagus and esophagogastric junction was completed using a standard fiberoptic system (Pentax FG34JH). Esophageal retention of a liquid or solid residue, status of the esophageal mucosa, and the presence or absence of resistance at the esophagogastric junction were noted.

Operation

Four patients had been submitted to a hydrostatic dilation before operation. One had a single session and 3 patients underwent two attempts at dilating the LES area. After their preoperative assessment all patients underwent a modified Heller myotomy through a left thoracic approach.

The esophagus was mobilized completely, from the inferior pulmonary vein in patients with achalasia and from the inferior border of the aortic arch in patients with diffuse spasm. Hiatal attachments were taken down, and mobilization of the whole gastric fundus was obtained by ligation of short gastric vessels. Exposure of the proximal stomach and subdiaphragmatic esophagus was usually afforded by a peripheral diaphragmatic invasion 2 to 3 cm from its chest wall insertion. A 56F Maloney bougie was used as an esophageal stent during the completion of myotomy. The muscle incision was prolonged caudally on the gastric wall musculature for 1 cm. The muscularis was then dissected free from the mucosa over 50% of the esophageal circumference. The muscular flap thus raised was cut transversally at its distal end and was everted at the gastroesophageal junction to prevent any healing of the myotomy. With the 56F Maloney bougie still in place a short 1- to 2-cm total fundoplication was completed. Three stitches of 2-0 silk reapproximated the anterior fundic wall to the posterior fundic wall while anchoring it to the everted muscle underneath. The distal esophagus and the periesophageal fundic wrap were then reduced under the diaphragm to which they were fixed by three sutures tied on the thoracic side of the hiatus. The posterior hiatus was left untouched.

Statistical Analysis

Student's t test for paired and unpaired values was used when appropriate. A p values less than 0.05 was considered statistically significant.

Table 2. Radiology and Radionuclide Transit

Variable	Preop	0–24 mo	25–48 mo	49–72 mo	73–120 mo
Radiology					
Transverse diameter	3.9	4.16	5.1	5.7	6.04
Stasis	12/17	12/17	6/9	7/9	10/10
Abnormal contractions					
Active	10/17	. . .	. . .	. . .	. . .
Atony	. . .	12/17	6/9	7/9	10/10
Radionuclide transit studies					
% Retention at 2 minutes (10-mL liquid bolus)	32.4 ± 31.8	29.2 ± 29	68.7 ± 30.6	53.7 ± 36.4	75 ± 7

Results

Clinical Evaluation

All 17 patients initially complained of dysphagia. Regurgitation episodes were present in 7. Three patients experienced episodes of aspiration. Clinical findings are summarized in Table 1. Symptoms decreased appreciably immediately after the operation. During the early months all patients were asymptomatic. At 24 months, however 5 of 17 patients or 29% of the whole group revealed symptoms. One patient had dysphagia and another felt a slow emptying of the esophagus. Three showed episodes of regurgitation. At 48 months 25% of the whole group had poor emptying symptoms and another 25% showed regurgitation episodes. Between 49 and 72 months, 21% of the group (3/14) had dysphagia or poor emptying and 35% had regurgitation episodes. Among 12 patients who were followed up from 73 to more than 120 months only 3 patients remain totally asymptomatic.

Five patients had to be reoperated on, all because of serious esophageal emptying problem and related symptoms. Of these 5 patients 2 underwent an esophagectomy with a short colon interposition at 38 and 62 months after their initial operation. Two more had an esophagectomy with gastric interposition at 66 and 74 months after the initial myotomy. In 1 patient the unwrapping of the fundoplication was performed through an upper abdominal approach.

Radiology

Table 2 summarizes the radiological and isotope transit study findings. Preoperatively the largest transverse diameter of the distal esophagus was 3.9 cm. Twelve of the 17 patients showed transient to prolonged stasis in the esophageal body. Tertiary contraction or hypomotility was noted in 10 of the 17 patients, and a small hiatal hernia was present in 1 of the 4 patients with a diagnosis of diffuse esophageal spasm.

After operation progressive esophageal dilation was observed. In 18 patients assessed radiologically during the initial 24 months of evolution the transverse esophageal diameter increased to 4.1 cm. In 9 patients evaluated after up to 48 months and in 9 assessed between 49 and 72 months, the transverse diameter increased from 4.1 to 5.1 and 5.7 cm, respectively. Ten patients had an esophagogram between 80 and 152 months of evolution, and their mean esophageal diameter was 6.04 cm. Similarly atony, stasis, and retention accompanied the characteristic imprint of the fundoplication on the distal esophagus and proximal stomach. All 17 patients at some point of their evolution showed these characteristics to some degree. Three are considered to have only transient hesitation and stasis, and 2 show satisfactory esophagogastric transit despite hesitation in the distal esophagus.

Esophageal Radionuclide Transit Study

Esophageal retention of the liquid bolus increased in parallel to the progressive dilatation and stasis observed radiologically. Before the operation, 32% of the radioactivity was retained at 2 minutes. Postoperatively esophageal retention at 2 minutes was 29% during the initial 24 months of evolution. Retention increased progressively over time. It was 68% during the period between 25 and 48 months, 53% when assessed between 49 and 72 months, and 75% in those patients studied between 73 and 152 months postoperatively.

Table 3. Preoperative and Postoperative Manometric Changes

Esophagus	Preop	Postop	p Value
Proximal			
Resting (mm Hg)	10.5 ± 5.36	4.48 ± 4.96	0.002
Peak (mm Hg)	38.4 ± 8.33	30.1 ± 8.75	0.005
Primary waves (%)	8.23 ± 20.38	38.9 ± 36.7	0.002
Spontaneous tertiary activity (No./min)	3.78 ± 2.62	0.94 ± 1.22	0.003
Distal			
Resting (mm Hg)	12.2 ± 7.02	4.62 ± 4.75	<0.001
Peak (mm Hg)	49.2 ± 22.7	28.1 ± 10.8	<0.001
Primary waves (%)	6.47 ± 24.2	5.29 ± 19.4	NS
Spontaneous tertiary activity (No./min)	3.32 ± 2.67	1.38 ± 1.75	<0.01
LES			
Gradient (mm Hg)	25.5 ± 10.5	7.45 ± 3.62	<0.001

LES = lower esophageal sphincter; NS = not significant.

Table 4. Long-Term Manometric Changes After Myotomy and Total Fundoplication

Esophagus	Up to 24 mo	25–48 mo	49–72 mo	73–120 mo	Correlation
Proximal					
Resting (mm Hg)	4.03 ± 4.64	6.71 ± 4.68	6.3 ± 4.59	12.6 ± 8.62	0.48
Peak (mm Hg)	28.4 ± 8.67	28.0 ± 7.37	30.1 ± 9.24	41.2 ± 18.7	0.267
Primary waves (%)	38.3 ± 37.1	27.4 ± 42.2	27.4 ± 33.6	51.8 ± 33.6	0.083
Spontaneous tertiary activity (No./min)	0.86 ± 1.46	0.85 ± 1.33	1.38 ± 1.71	0.42 ± 0.80	−0.018
Distal					
Resting (mm Hg)	4.40 ± 4.49	7.62 ± 6.86	7.68 ± 4.96	14.7 ± 8.34	0.468
Peak (mm Hg)	27.0 ± 9.66	30.51 ± 11.7	24.2 ± 5.02	20.0 ± 5.71	−7.29
Primary waves (%)	5.20 ± 18.5	1.11 ± 3.33	4.54 ± 8.20	2.5 ± 6.12	−9.0
Spontaneous tertiary activity (No./min)	1.10 ± 1.54	0.63 ± 0.78	0.94 ± 1.01	0.62 ± 0.72	−0.79
LES					
Gradient	6.68 ± 3.96	5.75 ± 2.81	7.54 ± 2.97	8.9 ± 5.58	0.05

LES = lower esophageal sphincter.

Manometry

Table 3 summarizes all preoperative and the first postoperative recorded manometric information in all patients. Table 4 shows the manometric changes over time after the operation.

In the proximal esophagus resting and peak contraction values were significantly altered by the operation. The resting pressure decreased significantly from 10.5 to 4.48 mm Hg and the peak pressure also decreased from 38 to 30 mm Hg. The incidence of peristaltic waves in response to swallowing increased from 8.2% preoperatively to 38.9% after the operation. When analyzed over a long period of observation, however, the resting pressure in the proximal esophageal body showed a progressive increase: in the immediate postoperative period resting pressures were 4.0 mm Hg, and they increased to 6.7 mm Hg at 48 months, to 6.3 mm Hg at 72 months, and to 12.6 mm Hg at 120 months.

In the distal half of the esophagus the resting pressures were also significantly reduced by the myotomy (from 12.2 to 4.6 mm Hg). The peak contraction pressures were reduced significantly as well by the operation from 49.2 to 28.1 mm Hg. The incidence of tertiary contractions remained unchanged by the operation. Over the years the resting pressures of the distal esophageal body increased progressively from 4.4 mm Hg immediately postoperatively to 7.6 mm Hg at 48 months, 7.6 mm Hg at 72 months, and finally 14.7 mm Hg at 120 months. Absolute resting pressures in the gastric cavity were substracted from absolute resting pressures in the lower esophageal sphincter to obtain the pressure gradient between esophagus and stomach. The resting pressure gradient in the lower esophageal sphincter area was reduced from 25.5 mm Hg before the operation to 7.4 mm Hg after myotomy and total fundoplication. This pressure gradient remained at the same level over the years of follow-up.

24-Hour pH Recording

Twenty-four–hour pH studies were obtained only during the postoperative evolution in this group of patients when the technique became available in the unit. Eight patients underwent 24-hour esophageal pH recordings. None actually showed any substantial exposure to acid in their esophagus. The details of their respective recordings are contained in Table 5.

Endoscopy

Preoperatively the resistance of the esophagus to passage of the endoscope was the most frequent feature in this group of patients. This resistance was usually located at

Table 5. Twenty-four–Hour pH Recording

Patient No.	Date	Months Postop	Episodes of Reflux	Minutes of Exposure to Acid	Episodes of Reflux > 5 min	Longest Total Reflux Episode (min)	Total % Exposure to Acid
1	4/89	105	0	0	0	0	0
2	7/91	132	10	4	0	0	0
3	3/89	111	1	0	0	0	0
4	12/89	80	45	9	0	0	1
5	8/86	92	1	0	0	0	0
	7/91	152	52	40	2	12	3
6	11/89	72	30	35	3	10	3
7	9/86	42	6	2	0	0	0

Table 6. Endoscopy

Variable	Preoperative (n = 17)	24 months (n = 16)	48 months (n = 10)	72 months (n = 12)	120 months (n = 8)
Dilatation	6	13	9	9	4
Retention					
Liquids	5	8	5	7	3
Solids	5	2	3	4	2
Resistance	15	0	0	0	0
Mucosa	Hyperemia, 2	Normal	Thickened, 1	Thickened, 2	Thickened, 2

the tight esophagogastric junction in patients with achalasia, but it was also noticed at the junction of the proximal and midesophageal body in those patients with esophageal spasm. Dilatation of the esophageal lumen was seen in one third of the group as were retained liquids and solids in the esophagus. The mucosa was hyperemic in 2 patients. In the postoperative follow-up, during the early months 13 of 16 patients assessed showed mostly dilatation, with 50% of the group showing saliva retention. Two had food particles in their esophageal body. After 48 months of evolution 9 of 10 patients who underwent endoscopy showed dilatation, with again 50% of the group showing saliva retention and 3 food particles in the esophageal body. The same observations were reported at 72 months and 120 months. At no time was there any resistance to the passage of the endoscope at the esophagogastric junction where the fundoplication could be viewed as intact by its typical mucosal folds in the subcardial region. With long-term evolution, the mucosa of the distal esophagus showed a thickened aspect in approximately 20% of the group. None of the 17 patients presented any evidence of any type of reflux esophagitis damage during the postoperative evolution (Table 6).

Comment

Palliation is the main goal of operation for primary motor disorders. Comfort during swallowing without the unpleasantness of obstruction, pain, and regurgitation must be offered to patients with these conditions. Persistent symptoms from an unsatisfactory esophagogastric transit or the appearance of heartburn from reflux disease must be considered failures of the surgical treatment.

The physiological changes of esophageal myotomy have been reported by Little [2], Csendes [3], Henderson [4], Ellis [5], Duranceau [6], and their associates. The LES high-pressure zone is decreased significantly by the operation. The pressure gradient decrease from 25.5 to 7.4 mm Hg in the LES for the present group represents a significant response to myotomy. The level of this remaining pressure barrier remains very stable over the years that follow. In the esophageal body a significant decrease in resting pressures and contracting pressures occurs immediately after the operation. Over time, however, the resting pressures will show a progressive increase both proximally and distally while the peak contraction pressures in the esophageal body remain weak. Csendes and associates [3] observed an increased incidence of propulsive waves after myotomy. Our earlier study [6] also showed reappearance of propulsion but only in the proximal half of the esophagus. The present group of patients with long-term follow-up shows that over time contractions in response to swallowing remain propulsive in the same area proximal to the myotomy. However, the distal half of the esophagus remains powerless and aperistaltic with a progressive increase in resting pressures suggesting retention.

The true incidence of reflux disease after myotomy for motor disorders is still a matter of controversy. Both in the older and more recent literature reflux damage in 3% to 52% of myotomized patients is reported [1]. There are advocates of a surgical myotomy alone, straddling the esophagogastric junction and extending onto the stomach for no more than 0.5 to 1 cm (Ellis and colleagues [5], Okike and co-workers [7]). Their claim is that the myotomy decreases sufficiently the LES resting pressures while leaving enough of a pressure gradient to protect against long-term reflux. Long-term results with objective documentation of the reflux incidence are lacking, however. Those who propose an added antireflux operation to myotomy argue that a high incidence of reflux occurs after removing or decreasing the LES pressure zone. Belsey [8], Peyton [9], Yon [10], Jara [11], Menzies-Gow [12], and their associates emphasize that extension of the myotomy low on the stomach increases the chances of exposure to the damaging reflux.

If the option of adding an antireflux operation is retained, the type of repair is still a matter of controversy. Effler [13], Belsey [8], Mansour [14], Gallone [15], Little [2], Csendes [3], Beauchamp [16], Hiebert [17], and their associates have proposed partial fundoplications with good control of reflux episodes. Rossetti [18], Holchuli [19], Menguy [20], Del Genio [21], Henderson [4], Duranceau [6], Stipa [22], and their associates have used total fundoplication. The failure rate was 11.3% in patients receiving a total fundoplication after myotomy. The failure rate was 9.5% when a partial fundoplication was added to the myotomy. The failure is caused by obstructive symptoms in patients with a total fundoplication. Reflux esophagitis symptoms are responsible for the failures in patients with partial fundoplications. Both Henderson and Ryder [4] and Veiga-Fernandes and associates [24] found minimal differences in the early follow-up of patients with myotomy and total fundoplication when compared with patients with a partial fundoplication. This was also our impression after assessing myotomy and total fundoplication early after the operation [6]. Thus the length of follow-up seems to be a major factor in the assessment of these patients.

This long-term observation of a limited group of patients with motor disorders shows that a total fundoplication added to a freshly myotomized esophagus is an inappropriate operation. Despite good reflux control, the functional obstruction created by the total fundic wrap results in progressive esophageal dilatation and retention. Poor emptying symptoms result. A 29% reoperation rate over time is not acceptable in treating these conditions. When reflux disease is to be prevented after myotomy for motor disorders, total fundoplication should be ruled out as an option.

Doctor Topart was supported by the Fondation pour la Recherche en Chirurgie de Montréal, Départment de Chirurgie, Hôtel-Dieu de Montréal, and the Ligue Française Contre le Cancer, France.

Appreciation is given to Mrs Gisele Bergeron for typing the manuscript.

References

1. Jamieson GG, Duranceau A. Reoperative surgery for problems after oesophagomyotomy. In: Jamieson GG, ed. Surgery of the oesophagus. London: Churchill Livingstone, 1988:797–802.
2. Little AG, Soriano A, Ferguson MK, Winans CS, Skinner DB. Surgical treatment of achalasia: results with esophagomyotomy and Belsey repair. Ann Thorac Surg 1988;45:489–94.
3. Csendes A, Braghetto I, Mascaro J, Henriquez A. Late subjective and objective evaluation of the results of esophagomyotomy in 100 patients with achalasia of the esophagus. Surgery 1988;104:469–75.
4. Henderson RD, Ryder DE. Reflux control following myotomy in diffuse esophageal spasm. Ann Thorac Surg 1982;34:230–6.
5. Ellis FH Jr, Crozier RE, Watkins E Jr. Operation for esophageal achalasia. Results of esophagomyotomy without an antireflux operation. J Thorac Cardiovasc Surg 1984;88:344–51.
6. Duranceau A, Lafontaine ER, Vallieres B. Effects of total fundoplication on function of the esophagus after myotomy for achalasia. Am J Surg 1982;143:22–8.
7. Okike N, Payne WS, Neufeld DM, Bernatz PE, Pairolero PC, Sanderson D. Esophagomyotomy versus forceful dilatation for achalasia of the esophagus: results in 899 patients. Ann Thorac Surg 1978;28:119–25.
8. Belsey R. Functional diseases of the esophagus. Cardiovasc Surg 1966;52:164–88.
9. Peyton MD, Greenfield LJ, Elkins RC. Combined myotomy and hiatal herniorraphy: a new approach. Am J Surg 1974;128:786–90.
10. Yon J, Christensen J. An uncontrolled comparison of treatments for achalasia. Ann Surg 1975;182:672–6.
11. Jara FM, Toledo-Pereyra LH, Lewis JW, Magilligan DJ Jr. Long term results of esophagomyotomy for achalasia of esophagus. Arch Surg 1979;114:935–6.
12. Menzies-Gow N, Gummer JWP, Edwards DAW. Results of Heller's operation for achalasia of the cardia. Br J Surg 1978;65:483–5.
13. Effler DB. Reconstruction of the esophageal hiatus. Arch Surg 1962;85:599–606.
14. Mansour KA, Symbas PN, Jones FL, Hatcher CR. A combined surgical approach in the management of achalasia of the esophagus. Am Surg 1976;42:192–5.
15. Gallone L, Peri G, Galliera M. Proximal gastric vagotomy and anterior fundoplication as complementary procedures to Heller's operation for achalasia. Surg Gynecol Obstet 1982;155:337–41.
16. Beauchamp G, Toure CT, Devito M. Gastroesophageal reflux after myotomy for achalasia. In: Siewert JR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer-Verlag, 1988.
17. Hiebert CA. Long term follow up of patients with achalasia treated by myotomy and partial fundoplication. In: Siewert JR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer-Verlag, 1988.
18. Rossetti M. Oesophagocardiomyotomie und Fundoplication. Eine physiologische Operation bei Cardiospasmus und mega Esophagus. J Suisse Chir 1963;93:925–31.
19. Holchuli R, Allgower M. Zum Chirurgischen Vorgehen beim mega Esophagus. Helv Chir Acta 1966;33:33–42.
20. Menguy R. Management of achalasia by trans abdominal cardiomyotomy and fundoplication. Surg Gynecol Obstet 1971;133:482–4.
21. Del Genio A. Total fundoplication after myotomy for motor disorders. Geemo Annual Symposium, Montreal, 1991.
22. Stipa S, Iascone C, Moraldi A, et al. Esophagomyotomy with antireflux procedures for achalasia of the esophagus: clinical comparison of Nissen Fundoplication and Belsey M.K.IV. In: Siewert JR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer-Verlag, 1988.
23. Nelems JMD, Cooper JD, Pearson FG. Treatment of achalasia: esophagomyotomy with antireflux procedure. Can J Surg 1980;23:588–9.
24. Veiga-Fernandes F, Pinheiro MF, Guerreiro D. Cardiomyotomy associated with antireflux surgery in the treatment of achalasia. World J Surg 1981;5:697–702.

DISCUSSION

DR CLEMENT A. HIEBERT (Windham, ME): Dr Topart, despite your gloomy conclusion, you have given everybody something to cheer about. Champions of the Mark IV operation will feel smug in knowing all along that a loose fundoplication is less obstructing than a 365-degree collar, whereas those who espouse the Ellis approach of a limited myotomy will receive your report as evidence that *any* antireflux maneuver is bad for a gullet that behaves like a drainpipe. The question remains: What operation are you now doing for a primary repair and what do you recommend for a patient whose primary operation has failed?

This report reminds us that operations for achalasia ideally correct the obstruction without adding problems but, even at best, leave the patient with a torpid pump. Although the conclusions sound gloomy, all of us are cheered by the very fact of this meticulous, truly long-term, and conspicuously honest study.

DR TOPART: Thank you, Dr Hiebert. At present, we are using a partial fundic wrap, using the Belsey technique, after myotomy for either achalasia or diffuse esophageal spasm.

In answer to your question on patients in whom total fundoplication failed, 5 patients had to be reoperated on: 3 had diffuse esophageal spasm and 2, achalasia. In one patient, 2 years after the myotomy and fundoplication an antrectomy and Roux-en-Y was performed by another surgeon for bile reflux gastritis. This same patient, when reoperated on for symptoms of obstruction by the fundoplication at 5 years after the myotomy, had at that point her fundoplication undone and a bilateral vagotomy added. She is now asymptomatic. The 4 remaining patients required resection and esophageal replacement using colon in 2 and stomach in 2.

DR TOM R. DEMEESTER (Los Angeles, CA): I, too, would like to compliment Dr Duranceau and Dr Topart on this very excellent study, and particularly because of their insistence on the use of physiological studies before the initiation of therapy. It is only by this means that follow-up studies on these patients can give insight into the effects of operation on the natural history of this disease. It also emphasizes that we cannot depend on symptomatic assessment as an indicator of success in achalasia. Many of these patients are able to adjust their eating habits to a substantial degree to avoid the symptom of dysphagia and hide the fact that the result has not been as successful as one would expect. Your studies will put an end to the notion that one can do a Nissen fundoplication to protect against reflux after a myotomy for achalasia, ie, disease where there is poor propulsion. This holds not only for achalasia but also for patients who have lost esophageal peristalsis from reflux disease. It takes us a long time to uncover the detrimental effect of a full fundoplication, but you have done so elegantly and by persistence in obtaining studies over a 10-year follow-up.

Have you noticed that in patients who have had too tight or too long an antireflux repair similar contractile findings develop in the body of the esophagus, and is there a reversal of those changes when the repair is taken down? Our studies in this situation indicate that once function of the body of the esophagus is lost, it is very difficult to get it back, regardless of the cause of the outflow obstruction, ie, failure of a relaxed valve or too tight a repair. Again, let me congratulate you on an excellent study and one that will affect the care of our patients.

DR TOPART: Thank you, Dr DeMeester. I cannot answer your question, but maybe Dr Duranceau would have a comment to make.

DR DURANCEAU: Thank you, Dr DeMeester. In answer to your question, we have not looked at patients who lost the function in their esophageal body from outflow obstruction. However, we looked at two other categories of patients who had a similar operation with poor function in their esophageal body, but who do not seem to respond in the same way. The freshly myotomized esophagus, when immediately wrapped, obviously shows decompensation over the years. If you do the same operation on scleroderma patients with no propulsion, they react differently. They empty poorly but still show substantial acid exposure, despite the short total wrap.

If this operation is offered to patients who had achalasia treated by myotomy 2, 3, or 4 years previously, and who have started refluxing after their myotomy, they do not seem to present the same decompensation with a total fundoplication. Four of these patients are on follow-up, a number too small to reach any conclusion. The observation from this presentation allow us to conclude only on those patients who had a myotomy with a short total fundoplication added immediately in the same setting.

Clinical Manifestation of Mediastinal Fibrosis and Histoplasmosis

Douglas J. Mathisen, MD, and Hermes C. Grillo, MD

General Thoracic Surgical Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

We treated 20 patients thought to have mediastinal fibrosis secondary to *Histoplasma capsulatum*. All but 1 were symptomatic. The most common symptoms were dyspnea (8), hemoptysis (6), postobstructive pneumonia (5), and superior vena caval obstruction (2). Nine patients had severe stenosis of the trachea, carina, or main bronchus. Special stains identified *Histoplasma capsulatum* in surgical specimens in 9 patients. Surgical procedures were done for 18 of 20 patients (resection of subcarinal mass, 6; right middle and lower lobectomy, 5; carinal pneumonectomy, 4; esophagoplasty, 4; sleeve resection, 3 (with right main bronchus in 1, right lower and middle lobectomy in 1, and carina in 1); right upper lobectomy, 1; middle lobectomy, 1; and bronchoplasty of left main bronchus, 1. There were 4 deaths, 3 after complications of carinal pneumonectomy and 1 in a patient with tracheobronchial obstruction that could not be dilated. Two patients were treated with amphotericin and 4 with ketoconazole. Sclerosing mediastinitis secondary to histoplasmosis presents tremendous surgical challenges because of the intense fibrosis encountered. Bronchoplastic procedures are possible in spite of the intense fibrosis. High mortality rates after carinal resection may be encountered. The exact role of antifungal therapy is as yet undefined.

(Ann Thorac Surg 1992;54:1053–8)

Histoplasma capsulatum is a ubiquitous fungal organism present in the soil. Certain parts of the country are endemic for this organism. In endemic areas as many as 80% of the population are positive on skin test for *Histoplasma capsulatum* [1]. Despite the ubiquitous nature of this organism and widespread exposure, clinically significant infection with *Histoplasma capsulatum* is uncommon. Surgeons are involved to evaluate pulmonary nodules and enlarged, calcified hilar and mediastinal lymph nodes in asymptomatic patients.

Fibrosing mediastinitis is a well-documented sequela of exposure to *Histoplasma capsulatum* and mediastinal granuloma [2–4]. Fibrosing mediastinitis developed over a 2-year period in 34% of patients (11 of 31) with mediastinal granuloma at the Mayo Clinic [4]. The inability to grow the organism from biopsy specimens has led to the conclusion that this devastating condition is not the result of active fungal proliferation but is a hypersensitivity reaction to healed infection. The delayed hypersensitivity results in intense inflammation in parenchymal foci and the draining lymph nodes leading to focal caseous necrosis. Healing occurs by encapsulation with fibrous tissues. It has been proposed that ongoing seepage of antigens from the necrotic center of the granuloma stimulates the process to continue in the rare patient who is especially hypersensitive. Of importance, fibroblasts are stimulated in normal tissues adjacent to the nodule, resulting in destruction of these tissues by what appears to be invading fibrosis [5]. Regardless of the etiology of this unusual phenomenon the consequences to patients can be devastating. Mediastinal fibrosis secondary to exposure to *Histoplasma capsulatum* is the most common benign cause of superior vena cava syndrome [6, 7]. Involvement of the tracheobronchial tree by intense fibrosis can lead to stenosis at all levels of the airway [2, 8, 9] (Fig 1). Esophageal obstruction has been caused by this process, as have esophagorespiratory fistulas [4] (Fig 2).

Even though *Histoplasma capsulatum* infection is a benign infection, when the advanced stage of mediastinal fibrosis is reached, it can have life-threatening implications for patients. The dense fibrosis that is present is often invasive into vital mediastinal structures and obliterates normal tissue planes. There is no medical treatment for this stage of the disease, and steroids are ineffective in reversing the fibrosing process. Surgical intervention is required to manage the complications of mediastinal fibrosis. The invasive nature of the intense fibrosis makes dissection technically difficult and hazardous. Surgeons must be aware of this advanced stage of the disease and the surgical options available.

Material and Methods

The hospital records of the Massachusetts General Hospital were reviewed from 1971 to 1991. Twenty patients with varying degrees of mediastinal fibrosis presumed to be secondary to *Histoplasma capsulatum* were seen during that period. Follow-up data were obtained by review of office records and telephone calls to patients and their families.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Mathisen, Massachusetts General Hospital, Boston, MA 02114.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Results

Patient Demographics

There were 10 women and 10 men. Their ages ranged from 18 to 63 years. The majority of patients were in their fourth or fifth decade of life. All patients were born and raised or lived for a substantial period of time in endemic areas of histoplasmosis. Those patients not raised in endemic areas spent at least 5 years in endemic areas during their third and fourth decade of life.

Radiologic Findings

All patients had abnormal chest roentgenograms. The most common finding was a large calcified hilar or subcarinal mass. Computed tomography was very helpful in defining the extent of the process and structures involved. Plain airway tomography was useful in defining the linear extent of airway involvement. Barium esophagogram demonstrated extrinsic compression in 5 patients and a communication with subcarinal nodes in 1 patient. Bilateral arm venograms were done in those patients suspected to have superior vena cava syndrome.

Signs and Symptoms

All but 1 patient had symptoms. Symptoms resulting from complications of airway involvement were the most common, including dyspnea (8), hemoptysis (7), and postobstructive pneumonia (5). Three patients with advanced airway obstruction required dilation to improve their airway. Superior vena cava syndrome was present in 2 patients. This was of gradual onset in both patients, and extensive collaterals had developed to lessen their symptoms. One patient had sepsis. There were no patients in our series who were seen with acute infectious histoplasmosis or for evaluation of solitary pulmonary nodules. This undoubtedly reflects that our institution is not located in an endemic area of histoplasmosis.

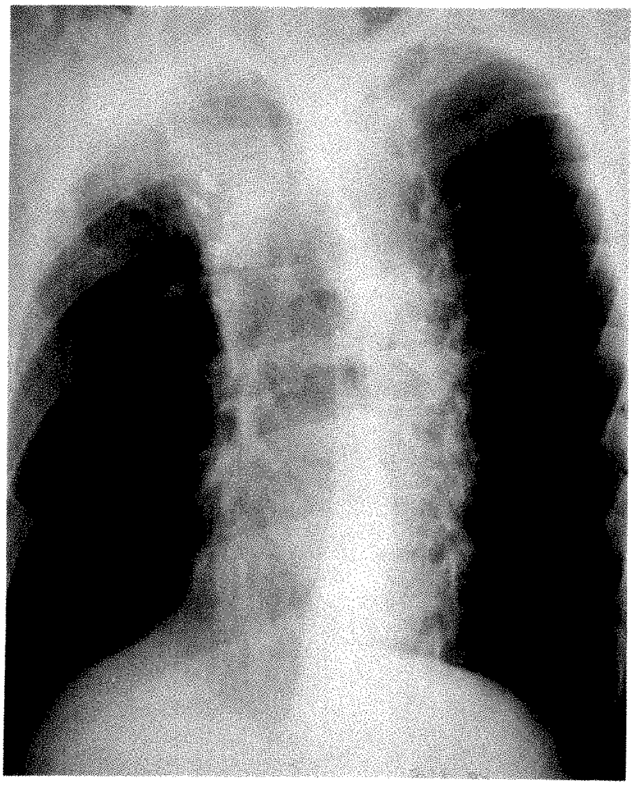


Fig 1. Oblique chest roentgenogram showing diffuse narrowing of the distal trachea, carina, and main bronchi.

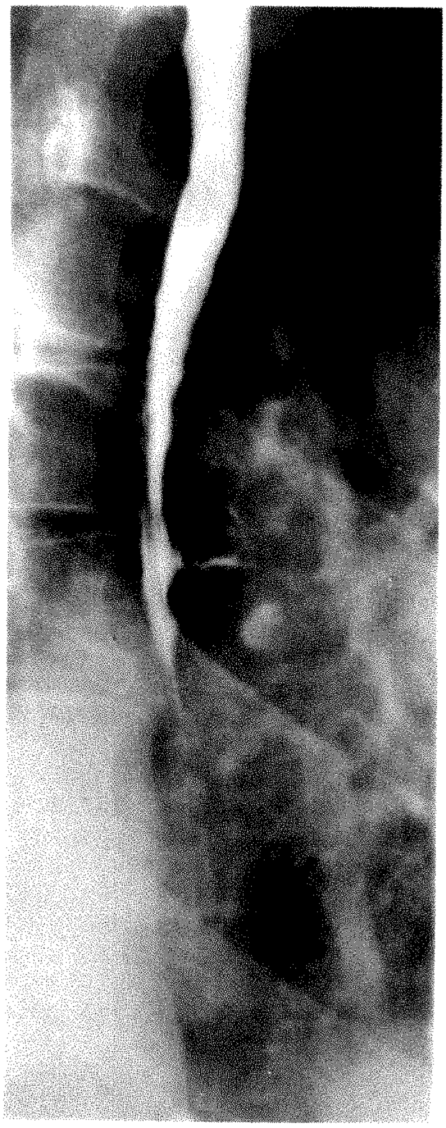


Fig 2. Barium swallow showing a small midesophageal fistula communicating with subcarinal lymph nodes.

Prior Operations

Seven patients had undergone prior thoracotomy up to 11 years before evaluation. Three patients underwent exploratory thoracotomy and biopsy only. They were deemed to have unresectable disease at the time. Broncholiths were removed in 2 patients without loss of pulmonary tissue. Progressive fibrosis and obstruction of the bronchus intermedius developed in both patients 3 and 5 years later. Middle lobectomy was performed in 1 patient for middle lobe syndrome. One patient had exploratory thoracotomy and decortication for empyema. No fungal organisms were cultured, but granulomas were identified in the pleura.

Medical Treatment

Steroid therapy was started in 6 patients once the diagnosis of mediastinal fibrosis was made. This therapy was instituted to minimize fibrosis but was considered ineffective in all patients. Two patients were given amphotericin at other institutions for presumed *Histoplasma* infection. One of the patients had an empyema and received a full course of treatment despite no organisms being cultured. The other patient was started on a regimen of amphotericin when organisms were seen on a biopsy specimen. Administration of amphotericin was discontinued after 1 week of therapy. Four patients were given ketoconazole postoperatively on the basis of organisms being seen in the resected specimen. Therapy was given for 3 months and terminated at that point. Three of the patients have remained in stable condition with no progression of their disease. Further involvement of the pulmonary artery to the right upper lobe developed in the fourth patient after right lower and middle lobectomy.

Skin and Serologic Testing

Only a small number of patients were tested for exposure to *Histoplasma*. Of those tested, only 1 had a negative serologic test for *Histoplasma*. Four patients had positive complement fixation tests for *Histoplasma* and 6 patients had positive skin tests.

Operative Procedures

Eighteen of 20 patients underwent operative procedures. One patient had severe airway obstruction secondary to stenosis of the distal trachea, carina, and right and left main bronchi. Emergency bronchoscopic dilation was attempted but the patient could not be ventilated and died in the operating room. One patient had superior vena cava syndrome. Her symptoms were mild. Consideration was given to bypassing the obstructed superior vena cava, but the patient declined and has been lost to follow-up. Six patients underwent resection of a large, calcified subcarinal mass. Right middle and lower lobectomy was done in 5 patients. All had symptoms of stenosis of the bronchus intermedius and lobar orifices. Three of the 5 patients had postobstructive pneumonia secondary to stenosis of the bronchus intermedius. Extensive fibrosis involving the mediastinum and hilar structures was found in all patients, requiring intrapericardial control of the pulmonary veins in 3 patients. Right upper lobectomy was done in 1 patient and right middle lobectomy in 1 patient for middle lobe syndrome. One patient had involvement of the left main bronchus by a large subcarinal mass. Removal of this mass required primary closure of a 5-mm hole in the left main bronchus.

Bronchoplastic procedures were done in 9 patients. All patients had dense fibrosis involving the airway but were amenable to bronchoplastic techniques. Four patients had right carinal pneumonectomy with anastomosis between the distal trachea and left main bronchus. One patient had an extensive carinal resection and reconstruction of the distal trachea to distal left main bronchus and right main bronchus to the side of the trachea. Because of the extent of the resection, the trachea had been divided in the neck to allow devolvement of the trachea into the mediastinum to allow primary anastomosis between the trachea and left main bronchus. Sleeve lobectomy was done in 3 patients. Two patients had right upper lobe sleeve lobectomy and 1 patient had sleeve middle and lower lobectomy with anastomosis between the right main bronchus and right upper lobe bronchus. In 1 patient the area of involvement was confined to the right main bronchus. The right main bronchus was resected and anastomosis was done between the side of the trachea and the distal right main bronchus. All bronchoplastic procedures included wrapping the anastomosis with either a pleural flap or pericardial fat pad.

Four patients had involvement of the esophagus by the subcarinal mass or mediastinal fibrosis. Excision of a small portion of the muscular wall of the esophagus was done in 2 patients with reapproximation of the muscle layers. One patient had a small full-thickness portion of the esophagus resected with two-layer primary closure performed. One patient had an acute febrile illness and enlarged, calcified subcarinal lymph nodes. Biopsy of the nodes revealed granulomas and cultured *Streptococcus viridans*. The patient was given penicillin and rapidly defervesced. Barium esophagogram 3 days after presentation revealed a communication between the esophagus and subcarinal mass of calcified lymph nodes. The subcarinal mass was resected, and the communication to the esophagus was closed in two layers and buttressed with an intercostal muscle flap. Recovery was uneventful.

Operative Mortality

There were four perioperative deaths. One patient died during attempted bronchoscopic dilation. Three patients died after carinal resection. One patient previously mentioned died of airway obstruction after anastomotic separation. This patient had extensive involvement of the airway that was not dilatable. No other medical options existed for this patient. Two other patients died of either adult respiratory distress syndrome or bronchopneumonia after right carinal pneumonectomy. The anastomosis was intact in both patients.

Pathologic Findings

All patients had evidence of dense hyalinized fibrosis and enlarged calcified lymph nodes. Granulomas were identified in all but 1 patient. Nine of the 20 patients had positive methenamine silver staining for *Histoplasma capsulatum*.

Follow-up

One patient with superior vena cava syndrome has been lost to follow-up. Follow-up of the remaining patients is available from 1 to 9 years. All surviving patients had primary healing of bronchial and esophageal suture lines despite the presence of fibrosis. Progressive stenosis of the pulmonary arteries to the right upper lobe with minimal flow to this lobe has developed in 1 patient. Middle and lower lobectomy was done 2 years ago. *Histoplasma capsulatum* was identified by methenamine silver staining, and ketoconazole was given for 3 months. Ketoconazole therapy was reinstituted with the findings of minimal flow to the right upper lobe. The patient experiences shortness of breath with exercise. No further surgical intervention has been done at this time. One patient had resection of a large calcified subcarinal mass because of intermittent fevers and concern over the mass as the source of her fevers. Necrotizing granulomas and *Histoplasma capsulatum* were found on pathologic examination of the mediastinal mass. The patient recovered uneventfully from operation but recently has been placed on a regimen of ketoconazole for continued low-grade fevers. The patient has had symptomatic improvement on this therapy. There has been no radiographic change demonstrated. All remaining patients have had resolution of their symptoms and no further progression of their disease.

Comment

There are certain well-identified endemic areas for *Histoplasma capsulatum*. Based on histoplasmin delayed hypersensitivity testing it is estimated that approximately 22% of the United States population have been infected with the organism at one time or other [1]. In the highly endemic areas in the great river valleys of the eastern central United States, from Ohio west to Kansas and from Indiana south to Louisiana, more than 80% of the population are sensitized [1]. Institutions not located in these endemic areas may have patients with this problem because exposure may have been many years ago and patients may since have moved elsewhere or referrals may be made to institutions with a particular expertise in managing problems related to the late manifestations of this fungal infection.

The initial presentation in asymptomatic patients may be for evaluation of an abnormal chest roentgenogram showing a coin lesion or enlarged calcified hilar or mediastinal nodes. Approximately 40% of patients with mediastinal granuloma are asymptomatic [4]. Other radiographic findings depend on the extent of mediastinal fibrosis and involvement of nearby structures. Computed tomography, plain tomography of the airway, barium esophagogram, venograms, and magnetic resonance imaging all may be helpful in evaluating patients with advanced mediastinal fibrosis [10].

Specific diagnosis can be very difficult. Differential diagnosis includes tuberculosis, blastomycosis, lymphoma, sarcoidosis, syphilis, coccidioidomycosis, actinomycosis, and silicosis. Histoplasmin skin tests are of little diagnostic value because such a large percentage of the population is already sensitized. Complement fixation titers may be of value, especially if followed serially. Urschel and associates [11] suggest correlation of symptoms, sedimentation rate, and complement fixation titers to determine reinstitution of antifungal therapy in chronic smoldering histoplasmosis. Material obtained at biopsy usually will show granulomas. Silver methenamine stains may demonstrate organisms (9 of 20 in our series) in resected specimens. The absence of identifiable organisms does not exclude the possibility of *Histoplasma capsulatum* being the etiologic agent.

Medical therapy has been reserved for patients with acute documented histoplasmosis. Amphotericin has been used in these circumstances. Mediastinal fibrosis is usually a late manifestation of exposure to *Histoplasma* and not associated with active infection. Treatment with amphotericin has not proved of any benefit in such cases. Given the side effects of amphotericin, its use should be reserved for those patients suspected of active acute infection. We have recently begun using oral ketoconazole postoperatively in patients with *Histoplasma capsulatum* identified in biopsy material. Urschel and associates [11] have reported some success in patients with recurrent symptoms treated with ketoconazole. We also have had 1 patient in whom recurrent low-grade fevers developed 2 years postoperatively thought to be secondary to smoldering histoplasmosis. Ketoconazole has relieved her fevers and led to subjective improvement in her condition. Encouraged by this experience, minimal side effects, and the potential consequences of continued infection, we will continue to administer oral antifungal agents for 3 months after operation in patients with *Histoplasma capsulatum* identified in biopsy material. Urschel and associates [11] recommended therapy for 1 year.

Surgical intervention should be considered when patients have large asymptomatic mediastinal granulomas [4, 12]. Dines and colleagues [4] found that 34% of cases of mediastinal granulomas progressed to fibrosing mediastinitis within a 2-year period. Because of this finding and the difficulties encountered in patients with fibrosing mediastinitis, serious consideration should be given to excision of large asymptomatic mediastinal granulomas or at the earliest sign of symptoms.

The late complications of fibrosing mediastinitis may be devastating [13–17]. Involvement of the superior vena cava, tracheobronchial tree, esophagus, and great vessels can pose technically demanding problems. The fibrotic process is often dense and rigid, and it encases structures, making dilation extremely difficult. Tissue planes are often absent, making any surgical procedure challenging. Lobectomies and pneumonectomies may require intrapericardial control of the pulmonary arteries and veins, as was found in 7 of our patients. Advanced fibrosis involving the tracheobronchial tree can lead to severe narrowing with pinpoint airways and respiratory distress, as was present in 5 of our patients [2, 8]. The process may become so extensive that no surgical option exists, as was the case in at least 1 of our patients.

We have had no experience with vascular bypass for superior vena cava syndrome from fibrosing mediastinitis. Others have reported modest success using spiral vein grafts [17].

Our interest in airway problems probably accounts for the disproportionate number of patients in our series with major involvement of the tracheobronchial tree. Many of the patients with involvement of the major airways have small constricted lumens that are quite rigid. The role of dilation and bronchial stents has yet to be defined. Many patients have such dense fibrosis that dilation is impossible. If extensive airway involvement is present and dilation is impossible, consideration should be given to endobronchial stenting given the high operative mortality of carinal resection in this group of patients. Pulmonary conserving procedures should be done whenever possible. Indeed, 9 of our patients underwent bronchoplastic procedures including sleeve lobectomy (3), carinal resection (1), and pneumonectomy (4), and 1 patient had sleeve resection of the right main bronchus. All anastomoses healed primarily except for one. This patient had extensive involvement of the trachea, carina, and both main bronchi. No other alternatives existed for this desperate patient. Excessive tension after a complex reconstruction of her airway resulted in separation and airway obstruction. Principles of bronchoplastic surgery should be observed. Primary healing can be expected even in the presence of surrounding fibrosis.

The mortality experienced by 3 of our patients after carinal resection underscores the need to intervene before extensive airway involvement occurs. This may be one more argument for removing mediastinal granulomas before fibrosing mediastinitis develops.

Involvement of the esophagus has been documented by others [4]. Esophagorespiratory fistulas have been reported [4]. In our series, 4 patients had involvement of the esophagus. Whenever full-thickness involvement is encountered the defect should be closed in two layers and buttressed with an intercostal muscle flap or pericardial fat pad. The one fistulous communication between a subcarinal granuloma and the esophagus was successfully handled in this fashion.

Surgery will continue to be a part of the management of patients with mediastinal fibrosis. Early intervention should be considered to avoid the difficulties encountered with fibrosing mediastinitis. Operations required for the complications of fibrosing mediastinitis are technically challenging, but good results can be achieved even for bronchoplastic procedures.

References

1. Edwards LB, Acquaviva FA, Livesay VT, Cross FW, Palmer CE. An atlas of sensitivity to tuberculin, PPD-B, and histoplasmin in the United States. Am Rev Respir Dis 1969; 99(Suppl):1–132.
2. Schonengerdt CB, Suyemoto R, Main FB. Granulomatosis and fibrosing mediastinitis. A review and analysis of 180 cases. J Thorac Cardiovasc Surg 1979;57:365–79.
3. Hewett TH, Steer A, Thomas DE. Progressive fibrosing mediastinitis. Ann Thorac Surg 1966;2:345–57.
4. Dines DR, Bernatz PE, Pairolero PC. Mediastinal granuloma and fibrosing mediastinitis. Chest 1979;75:320–4.
5. Goodwin RA Jr, Nickell JA, Des Perez RM. Mediastinal fibrosis complicating healed primary histoplasmosis and tuberculosis. Medicine 1972;51:227–46.
6. Mahajan V, Strimlan V, Van Ordstran HS, et al. Benign superior vena cava syndrome. Chest 1975;68:32–4.
7. Parish JM, Marschke RF, Dines DE, et al. Etiologic considerations in superior vena cava syndrome. Mayo Clin Proc 1981;56:407–11.
8. James EC, Harris SS, Dillenburg CJ. Tracheal stenosis: an unusual presenting complication of idiopathic fibrosing mediastinitis. J Thorac Cardiovasc Surg 1980;80:410–3.
9. Zujtchuk R, Strevey TE, Heydorn WH, Treasure RL. Mediastinal histoplasmosis. J Thorac Cardiovasc Surg 1973;66: 300–4.
10. Skin MS, Kangh-Jey J. Computed tomography evaluation of bilateral bronchostenosis caused by sclerosing granulomatous mediastinitis: a complication of histoplasmosis. J Comput Tomogr 1984;8:345–50.
11. Urschel HC Jr, Razzuk MA, Netto GJ, Disiere J, Chung SY. Sclerosing mediastinitis: improved management with histoplasmosis titer and ketoconazole. Ann Thorac Surg 1990; 50:215–21.
12. Ferguson TB, Burford TH. Mediastinal granuloma. Ann Thorac Surg 1965;1:125–41.
13. Berry DF, Buccigrossi D, Peabody J, Peterson KL, Moser KM. Pulmonary vascular occlusion and fibrosing mediastinitis. Chest 1986;89:296–301.
14. Gryboski WA, Crutcher RR, Holloway JB, Mayo P, Segnitz RH, Eiseman B. Surgical aspects of histoplasmosis. Arch Surg 1963;87:590–9.
15. Light AM. Idiopathic fibrosis of the mediastinum: a discussion of three cases and review of the literature. J Clin Pathol 1978;31:78–88.
16. Prager RL, Burney DP, Waterhouse G, Bender HW Jr. Pulmonary, mediastinal, and cardiac presentations of histoplasmosis. Ann Thorac Surg 1980;30:385–90.
17. Doty DB. Bypass of superior vena cava. J Thorac Cardiovasc Surg 1982;83:3326–38.

DISCUSSION

DR THOMAS M. DANIEL (Charlottesville, VA): I congratulate Dr Mathisen and Dr Grillo on this presentation. This is quite a difficult disease to tackle. We come from a more endemic area. I also, for the interest of the audience, point out that about a year ago in the *New England Journal of Medicine* there was a CPC where Dr Grillo discussed one of these major carinal resections, and in understated surgical form—after the internist spent 4 or 5 pages discussing the disease—the surgeon just said, "And a simple carinal resection was made and the patient recovered uneventfully." That is an incredible achievement.

In view of some recent studies by Mr Peter Goldstraw from London about using stents inside the bronchus, when you have these high-risk carinal resections facing you, is it possibly a consideration to use one of the wall stents, these expandable medical stents that our vascular radiologists are using?

DR MATHISEN: Thanks, Dr Daniel, for your question; indeed, it is an insightful question, as many of these patients have extensive fibrosis and really do not have a surgical option. In those cases where extensive involvement is found, a stent would be preferable. Unfortunately many of these patients have a degree of inflammation and fibrosis that in our experience does not allow dilation. But if they do have a dilatable lesion and it is very extensive and you do not think a carinal resection is feasible, then I would agree either the Gianturco stents that you have alluded to or even the standard Silastic T tube would be a preferable alternative.

DR JOEL D. COOPER (St. Louis, MO): Having moved to an endemic area I have had a rapid course in this disease. It certainly makes all pulmonary resections more "sporting" than I had previously found them. I have a couple of questions for you. I think there is a question as to whether the calcified form of lymph node involvement and the more extensive, uniform fibrotic form are in fact the same disease or not, or whether one is an immunologic reaction to the disease. Your computed tomographic scan, for example, with the more pervasive fibrotic involvement did not show much calcification. That is also our experience. So I think there is a question as to whether the calcified node form of the disease and the extensive fibrosing mediastinitis are different phases or in fact different reactions, and I would like your thought on that.

The second question relates to stents, which I tend to favor when possible. If you look at your series, how many of the patients had operation for palliation of centrally obstructed airways? I understand that the lobectomies were probably for broncholiths, bleeding, and other problems, but how many of your operations were actually for strangulation due to airway obstruction of the trachea or main bronchi, and what were your results in that, certainly the most difficult, group of patients?

I very much enjoyed the presentation. This is a very challenging subject, one in which, in the middle west, you get a very quick course in this type of problem.

DR MATHISEN: One of the problems is that in many cases you are not able to document the cause of fibrosing mediastinitis and therefore it is somewhat of a leap of faith to go from granulomas to fibrosing mediastinitis. I think the most compelling observation is the one that I referred to from the Mayo Clinic, where they documented a group of patients with mediastinal granulomas, observed them, and over a 2-year period of observation found a 34% incidence of fibrosing mediastinitis developing. There have been many theories that have been postulated to explain how one goes from mediastinal granulomas to fibrosing mediastinitis, and indeed a hypersensitivity-type reaction is probably the most plausible explanation for this process, whereby the antigens contained within this calcified mass seep out, rupture, or whatever, and the body's immunologic response to it is this intense fibrotic reaction.

I cannot specifically answer how many of these patients had airway strangulation, but there were 6 patients who had carinal resections or resection of the main bronchus for airway obstruction. Of the 5 patients who underwent lobectomies, 3 had postobstructive pneumonias and the other 2 had collapse or prior infections. So indeed a number of these patients had airway obstruction. If you have a surgically resectable disease process I think it is preferable to resect it rather than using a stent, but when that is not possible I think stenting is indeed an acceptable alternative.

One more thing I might add is that of the patients who had major pulmonary resections, many had to be operated on intrapericardially, with intrapericardial control of the pulmonary artery and vein, indicative of the type of extension of this fibrosing process that you find.

DR RAYMOND A. DIETER, JR (Glen Ellyn, IL): Part of my comments have already been discussed. We have seen a number of individuals with primary carcinoma of the lung and mediastinal adenopathy or masses suggestive of rather extensive tumor metastasis to the mediastinum. Yet when we have explored these patients we have found that the adenopathy was due to histoplasmosis with viable *Histoplasma* organisms in nodes. I wonder if any of your patients had previous carcinoma resection or if this is a consideration that you might have had?

DR MATHISEN: None of our patients had prior carcinomas. Most often surgeons are asked to evaluate these mediastinal masses to rule out the presence of cancer, and I would guess that is the most common presentation to a thoracic surgeon who works in an endemic area.

Postcardiotomy Centrifugal Mechanical Ventricular Support

Leonard A. R. Golding, MD, Ray D. Crouch, MD, Robert W. Stewart, MD, Roberto Novoa, MD, Bruce W. Lytle, MD, Patrick M. McCarthy, MD, Paul C. Taylor, MD, Floyd D. Loop, MD, and Delos M. Cosgrove III, MD

The Cleveland Clinic Foundation, Cleveland, Ohio

From August 1979 through August 1991, 91 patients were supported with centrifugal mechanical ventricular assist. Major indications for its use were postcardiotomy ventricular failure (79) or as a bridge to cardiac transplantation (12). In postcardiotomy use (0.2% of all cardiac procedures), there were 54 male (68.4%) and 25 female patients (31.6%) with a mean age of 54.8 years and a mean duration of use of 3.56 days (range, 1 hour to 19 days). Forty-nine patients (62%) were successfully weaned, and 20 (25.3%) were hospital survivors. In 57 patients the device was inserted to wean from cardiopulmonary bypass, whereas in 22 it was employed later in the postoperative period because of low cardiac output or sudden arrest. Thirty-four (59.6%) of the 57 patients in the former group were weaned, and 15 (26.3%) were discharged, results similar to those in the latter group with 15 (68.2%) weaned and 5 (22.7%) discharged. Morbidity associated with use of centrifugal blood pumps included bleeding (87.3%; mean transfusion requirement, 53.2 units), renal failure (46.8%), cerebrovascular accident (12.7%), thromboembolism (12.7%), and hepatic insufficiency (12.7%). After a mean follow-up of 45.4 months (range, 2 to 142 months), 7 patients had died (35% late mortality), 1 patient is in functional class IV, and all others are in functional class I or II. Lower survival was associated with biventricular failure and renal failure but not with age or sex of the patient.

(Ann Thorac Surg 1992;54:1059–64)

The use of mechanical ventricular assist for postcardiotomy cardiogenic shock continues to increase and is instituted either as an aid to weaning from cardiopulmonary bypass or for patients whose condition deteriorates in the immediate postoperative period. This report summarizes our experience over the last 12 years with the use of nonpulsatile mechanical assist in patients with postcardiotomy cardiogenic shock.

Material and Methods

During the 12-year period from August 1979 through August 1991, centrifugal ventricular assist was employed in a total of 91 patients using either the Medtronic or the Bio-Medicus pump (Medtronic pump, Medtronic, Inc, Minneapolis, MN; Bio-Medicus Bio-Pump, Bio-Medicus, Eden Prairie, MN). This report excludes additional patients supported with roller pumps, the Nimbus Hemopump (Nimbus Medical, Inc, Rancho Cordova, CA), or pulsatile devices. The insertion of this device as a sole procedure to bridge to transplantation was performed in an additional 12 patients, and they also are excluded from this report. During the same period, 37,998 cardiac procedures employing cardiopulmonary bypass were performed at our institution, 1,114 (2.9%) of which required intraaortic balloon counterpulsation for successful weaning from cardiopulmonary bypass or in the postoperative period. More aggressive support in the form of left ventricular, right ventricular, or biventricular assist was required in 79 patients (0.2% of all cardiac operations), and they form the basis of this report.

The charts of all 79 patients who received ventricular support for postcardiotomy cardiogenic shock were retrospectively reviewed. Results were computed for all patients as a whole as well as for each category of left ventricular, right ventricular, and biventricular assist. Weaning from the ventricular assist device (VAD) and discharge from the hospital were analyzed with respect to age, position of the device (left, right, or biventricular), duration of assist, and evidence of perioperative infarction. Univariate and multivariate analyses of preoperative and day-of-wean values of creatinine, blood urea nitrogen, total bilirubin, serum glutamic-oxaloacetic transaminase, hematocrit, platelets, pH, oxygen tension, and carbon dioxide tension were done in an attempt to identify predictors of weaning and survival.

Our indications and contraindications for use of the VAD have remained consistent and are similar to those of others [1, 2]. The device is considered for a patient who does not respond to maximal drug support with inotropic agents and vasodilators, intraaortic balloon pumping, and at least 30 minutes of rest on full cardiopulmonary bypass. The 30-minute period also allows time for correction of any biochemical, hematologic or cardiac rhythm abnormalities.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Golding, Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

The device components and our techniques of insertion of the centrifugal assist device have been previously described [3]. The Bio-Medicus centrifugal pump is an inexpensive, readily available constrained-vortex pump that is easily adaptable to standard cardiopulmonary bypass tubing. Pump output is proportional to revolutions per minute and is capable of total circulatory support. Standard cannulation for left ventricular assist employs a 32F or 36F armored venous cannula introduced through the right superior pulmonary vein and secured with Teflon buttress sutures and tourniquets. Arterial cannulation is through the ascending aorta and in most cases uses the armored arterial cannula already in place. The cannulas are brought out through the inferior aspect of the incision or separate stab wounds. The patient is weaned from bypass as the pump flow is brought up to 2.2 $L \cdot min^{-1} \cdot m^{-2}$. A left atrial monitoring line is routinely placed. Evaluation of right heart function is critical, and if failure is present, it is managed first with infusions of isoproterenol hydrochloride or prostaglandin E_1. If this evokes no response, biventricular assist is considered. When stable hemodynamics are obtained, heparin sodium is reversed with protamine sulfate, and hemostasis is secured. Ideally the sternum or at least the skin alone is closed, but if this is not possible, a sterile dressing is placed and closure attempted after 24 hours. Cardiotonic agents are kept to a minimum, and intraaortic balloon pump support is continued until after the assist device is removed.

Postoperatively, mechanical ventilation and sedation are continued. When bleeding has been controlled, a continuous infusion of heparin is begun to maintain the activated clotting time at approximately 150 seconds and is increased to higher levels when flows are decreased during the process of weaning. Pump flows of at least 2.2 $L \cdot min^{-1} \cdot m^{-2}$ are maintained for a minimum of 24 hours.

Hemodynamic goals are a mean arterial pressure of 70 to 90 mm Hg, a left atrial pressure of 10 to 15 mm Hg, a central venous pressure of 10 to 15 mm Hg, a cardiac index of 2.4 $L \cdot min^{-1} \cdot m^{-2}$ (measured by Swan-Ganz thermodilution), and a systemic vascular resistance of 1,000 $dyne \cdot s \cdot cm^{-5}$ or less. Weaning is a gradual process of decreasing pump flows over a period of 12 to 24 hours, and when systemic flow can be maintained with pump flows of 500 $mL \cdot min^{-1} \cdot m^{-2}$ with stable systemic arterial and left atrial pressures, system removal in the operating room is scheduled.

Results

Patients ranged in age from 2 days to 73 years with a mean age of 54.8 years. There were 54 male patients with a mean age of 53.5 years (range, 2 days to 73 years), which differed only slightly from the mean age of 57.6 years (range, 50 to 72 years) for the 25 female patients. Cardiac procedures preceding placement of the VAD (Fig 1) were elective in 64 patients (81%) and emergent in 15 (19%).

Forty-nine (62%) of the 79 patients were successfully weaned from ventricular assist, but only 20 (25.3%) survived to be discharged from the hospital (Table 1). Isolated left ventricular support represented the largest proportion in our experience (47 patients, 59.5%) and yielded the best results, with 32 patients (68.1%) weaned and 14 (29.8%) discharged. Right ventricular assist alone (18 patients, 22.8%) resulted in 9 patients (50%) weaned and 4 (22.2%) discharged. The 14 patients (17.7%) who required biventricular assist fared much worse; although 8 (57.1%) were weaned, only 2 patients (14.3%) were discharged from the hospital. The difference in survival between patients supported with a left or right VAD (LVAD, RVAD) compared with those requiring biventricular assist devices (BVADs) was not significant ($p = 0.48$). Mortality after successful weaning and before hospital discharge was attributable to cardiac deterioration in almost all instances, although a few patients died of infection or stroke.

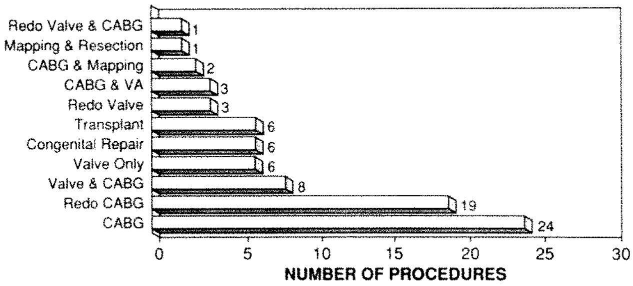


Fig 1. Types of cardiac surgical procedures preceding placement of ventricular assist device or devices. (CABG = *coronary artery bypass grafting;* VA = *ventricular aneurysmectomy.*)

When the operative procedure was elective (64 patients), 43 patients (67.2%) were weaned and 17 (26.6) were discharged. However, when the procedure was an emergency, only 6 (40%) of 15 patients were weaned and 3 (20%), discharged (Table 2). The difference between these two groups was significant for weaning ($p = 0.05$) but not for survival.

Fifty-seven (72.2%) of the 79 patients required mechanical support to be weaned from cardiopulmonary bypass. Thirty-four (59.6%) of them were weaned, and 15 (26.3%) survived to be discharged. The remaining 22 patients (27.8%) were initially weaned from bypass, stabilized, and transferred to the intensive care unit, but they required ventricular assist at variable periods after operation to treat ongoing cardiogenic shock or sudden arrest with

Table 1. Overall Results for Postcardiotomy Support[a]

Position	No. of Patients	Weaned	Discharged
LVAD	47	32 (68.1)	14 (29.8)
RVAD	18	9 (50)	4 (22.2)
BVADs	14	8 (57.1)	2 (14.3)
Total	79	49 (62)	20 (25.3)

[a] Numbers in parentheses are percentages.

BVADs = biventricular assist devices; LVAD = left ventricular assist device; RVAD = right ventricular assist device.

Table 2. Results for Elective Versus Emergency Procedures[a]

Procedure	No. of Patients	Weaned	Discharged
Elective	64	43 (67.2)	17 (26.6)
Emergency	15	6 (40)[b]	3 (20)

[a] Numbers in parentheses are percentages. [b] Significance: $p = 0.05$ compared with number weaned after elective procedure.

resuscitation and subsequent shock. Fifteen (68.2%) of them were weaned and 5 (22.7%), discharged. The difference in survival between these two groups was not significant ($p = 0.74$).

Mean duration of ventricular support for all patients was 3.56 days, but patients with BVADs required significantly longer periods of assist ($p = 0.04$) (mean duration, 6.75 days versus 3.69 days for patients with an LVAD and 2.78 days for those with an RVAD). The mean duration of assist for survivors and nonsurvivors was 3.35 days and 3.63 days, respectively, and proved not to be significant.

Age and sex were analyzed for their influence on weaning and survival. During this period, female patients constituted 24.1% of all cardiac surgical patients and almost one third of all patients with VADs and had a similar survival to male patients (24% versus 26%). Age had an effect on survival (Table 3) but only when considered as greater than or equal to 50 years and less than 50 years. The 8 patients 70 years old or older had a survival similar to that of the overall group (25% versus 25.3%).

Complications associated with the use of VADs were frequent (Fig 2). The most common complication was severe postoperative bleeding (87.3% of patients: LVAD, 89.4%; RVAD, 77.8%; and BVADs, 92.9%), which required massive transfusions of blood products (mean value, 53.2 units for the overall group). In comparison, 48.5% of all cardiac surgical patients in this same period required blood transfusions, and the mean value was 2.6 units per patient. For VAD patients, replacement was primarily packed red blood cells (mean value, 33.6 units) but also included fresh frozen plasma (mean value, 10.9 units), platelets (mean value, 7.1 units), and cryoprecipitate (mean value, 1.9 units). Patients supported with BVADs required more blood products (mean value, 65.5 units versus 50.8 and 49.5 units for patients with LVADs and RVADs, respectively), but this did not reach significance ($p = 0.19$).

The chest could not be closed initially in 48 patients (60.8%); 29 (61.7%) of the patients with LVADs, 10 (55.6%) of the patients with RVADs and 9 (64.3%) of the patients with BVADs. Despite this, mediastinitis occurred in only 10 patients (12.7%) (LVAD, 10.6%; RVAD, 5.6%; BVADs, 21.4%). Thirty-seven patients (46.8%) demonstrated varying degrees of renal insufficiency. This was significantly higher than the 2.3% incidence seen in all cardiac surgical patients during this period. Eleven (29.7%) required hemodialysis; 16 (43.2%), continuous arteriovenous hemofiltration; and 5 (13.5%), slow continuous ultrafiltration. Five patients died before the institution of dialysis or filtration therapy. Only 3 patients (8.1%) with renal insufficiency survived despite early and aggressive management. This low survival proved to be significant compared with the survival of the overall group ($p = 0.001$).

Table 3. Effect of Age on Weaning and Survival[a]

Age (y)	No. of Patients	Weaned	Discharged
<50	19	11 (58)	8 (42)
≥50	60	38 (63)	12 (20)[b]
≥70	8	5 (63)	2 (25)

[a] Numbers in parentheses are percentages. [b] Significance: $p = 0.005$ compared with age less than 50 years.

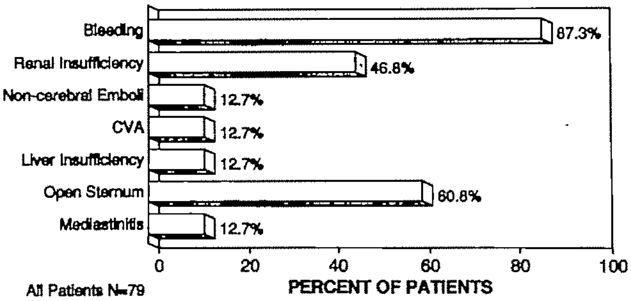


Fig 2. Morbidity after postcardiotomy mechanical support. (CVA = cerebrovascular accident.)

Cerebrovascular accident, embolic events other than those to the central nervous system, and hepatic insufficiency each occurred in 12.7% of patients. When separated by position of the VAD, the results were as follows: noncerebral emboli—LVAD, 14.9%; RVAD, 11.1%; and BVADs, 7.1%: cerebrovascular accident—LVAD, 6.4%; RVAD, 11.1%: and BVADs, 35.7%; liver insufficiency—LVAD, 8.5%; RVAD, 16.7%; and BVADs, 21.4%. Those patients supported with biventricular assist exhibited a higher incidence of postoperative morbidity in all categories except noncerebral emboli, but this proved significant only with respect to the incidence of cerebrovascular accidents ($p = 0.01$).

Univariate analysis (Wilcoxon rank sum test for continuous variables and Student's t test, χ^2 test, and Fisher's exact test for categorical data) of multiple laboratory values including blood urea nitrogen, creatinine, total bilirubin, serum glutamic-oxaloacetic transaminase, hematocrit, platelets, pH, oxygen tension, and carbon dioxide tension (obtained preoperatively and on the day of weaning) showed preoperative blood urea nitrogen as the only laboratory value with any predictive value for survival ($p = 0.04$). Both preoperative blood urea nitrogen and creatinine levels were significant in regard to weaning (both, $p = 0.05$). Multivariate analysis of these same variables failed to reveal any significant predictor.

Analysis of myocardial damage in survivors and nonsurvivors was done. Patients who died and on whom a postmortem examination was done showed marked myocardial damage in 68.6% (24/35). Among the survivors, 2

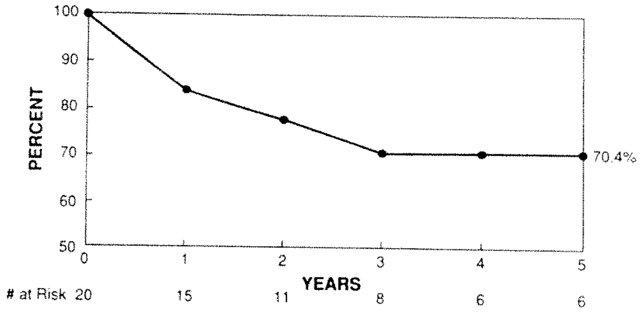


Fig 3. Kaplan-Meier survival curve for discharged patients.

had major injury and required transplantation for survival when weaning was not possible. For the remaining survivors, myocardial injury was documented in 50%.

Twenty patients were discharged from the hospital. In 2 (1 with an LVAD and 1 with BVADs), insufficient myocardial recovery occurred, and they could not be weaned. Both were accepted into the transplantation program and were discharged after getting new hearts. Follow-up data were obtained on 19 patients by clinic visit or telephone interview. One patient who was alive 2 months after discharge has since been lost to follow-up. The mean follow-up is 45.4 months with a range of 2 to 142 months.

Seven of the 20 patients discharged have died (late mortality of 35%), and Kaplan-Meier actuarial survival is 70% at 5 years (Fig 3). Five of the seven late deaths were cardiac in origin, one was due to carcinoma of the lung, and the cause of one is unknown. Eight of the 12 surviving patients are in New York Heart Association functional class I, 3 are in functional class II, and 1 is in functional class IV. The first patient successfully supported with ventricular assist at The Cleveland Clinic in 1979 [3] is now in his 80s and remains active.

Comment

Spencer and colleagues [4] and DeBakey [5] were the first to report the successful use of ventricular assistance in patients with postcardiotomy cardiogenic shock. The clinical application of VADs continues to grow, and multiple institutions have reported their experiences with several devices [6–16]. In addition to supporting the systemic or pulmonary circulation, or both, the pump unloads the failing ventricle, decreases myocardial oxygen demand, allows time for restoration of high-energy substrates and reduction of myocardial edema, and thereby allows recovery of the "stunned" myocardium [17, 18]. Our results for mortality and morbidity are similar to those of others [19]. The use of postcardiotomy mechanical support remains relatively limited [9–11, 16, 19], and survival remains almost the same despite the increasing complexity of cases and the increasing age of patients. Prolonged delay to initiation of support is now infrequent if the patient appears an appropriate candidate. In contrast to our earlier reports [1, 14], we now have found that the duration of support did not significantly differ between survivors and nonsurvivors and that one half of our survivors demonstrated some degree of permanent myocardial injury as evidenced by the electrocardiogram and cardiac enzymes.

Other authors [20, 21] have reported equal, if not improved, results with biventricular as opposed to univentricular assist. Our experience differs in that biventricular assist was associated with a lower survival and a higher incidence of postoperative morbidity of all types except noncerebral emboli. Statistical analysis, however, showed significance only for the frequency of cerebrovascular accidents. Analysis of multiple laboratory values showed renal dysfunction alone to be significant as a prognostic indicator of survival.

Age has been reported as a prognostic indicator by others [11, 19], with survival as low as 6% for patients older than 70 years. By contrast, in our series there was no difference in survival for patients 70 years old or older versus those less 70 years of age.

Several groups [22–27] have reported follow-up of 24 months or more for hospital survivors of mechanical circulatory support with late mortality ranging from 0% to 56%. Our late mortality of 35% at a mean follow-up of 3.8 years appears acceptable but demonstrates that hospital discharge alone is not predictive of long-term survival.

There is still no specific test to determine reversibility of cardiac dysfunction at the time of initiation of support. Severe biventricular failure and early renal failure denote a poor prognosis, and for survivors, the late cardiac-related mortality is higher than for patients surviving a cardiac operation with or without intraaortic balloon pump support. The low survival rate and the high associated costs in dollars and complications mean that selection of suitable candidates must be improved.

We thank Ms J. Borsh, RN, Department of Thoracic and Cardiovascular Research, and Greg Pearce, Department of Biostatistics, for their invaluable help.

References

1. Golding LAR. Postcardiotomy mechanical support. Semin Thorac Cardiovasc Surg 1991;3:29–32.
2. Pennington DG, Joyce LD, Pae WE Jr, Burkholder JA. Patient selection. Ann Thorac Surg 1989;47:77–81.
3. Golding LR, Groves LK, Peter M, et al. Initial clinical experience with a new temporary left ventricular assist device. Ann Thorac Surg 1980;29:66–9.
4. Spencer FC, Eiseman B, Trinkle JK, Rossi NP. Assisted circulation for cardiac failure following intracardiac surgery with cardiopulmonary bypass. J Thorac Cardiovasc Surg 1965;49:56–73.
5. DeBakey ME. Left ventricular bypass pumps for cardiac assistance. Clinical experience. Am J Cardiol 1971;27:3–11.
6. Park SB, Liebler GA, Burkholder JA, et al. Mechanical support of the failing heart. Ann Thorac Surg 1986;42:627–31.
7. Pierce WS, Parr G, Myers JL, Pae WE, Bull AP, Waldhausen JA. Ventricular assist pumping in patients with cardiogenic shock after cardiac operations. N Engl J Med 1981;205:1606–10.
8. Zumbro GL, Kitchens WR, Shearer G, Harville G, Bailey L, Galloway RF. Mechanical assistance for cardiogenic shock

following cardiac surgery, myocardial infarction, and cardiac transplantation. Ann Thorac Surg 1987;44:11–3.
9. Drinkwater DC, Laks H. Clinical experience with centrifugal pump ventricular support at UCLA Medical Center. ASAIO Trans 1988;34:505–8.
10. Ott RA, Mills TC, Eugene J, Gazzaniga AB. Clinical choices for circulatory assist devices. ASAIO Trans 1990;36:792–8.
11. Killen DA, Piehler JM, Borkon AM, Reed WA. Bio-Medicus ventricular assist device for salvage of cardiac surgical patients. Ann Thorac Surg 1991;52:230–5.
12. Rose DM, Colvin SB, Culliford AT, et al. Late functional and hemodynamic status of surviving patients following insertion of the left heart assist device. J Thorac Cardiovasc Surg 1983;85:639–45.
13. Karl TR, Sano S, Horton S, Mee RB. Centrifugal pump left heart assist in pediatric cardiac operations. J Thorac Cardiovasc Surg 1991;102:624–30.
14. Golding LAR, Jacobs G, Groves LK, Gill CC, Nose Y, Loop FD. Clinical results of mechanical support of the failing left ventricle. J Thorac Cardiovasc Surg 1982;83:597–601.
15. Noon GP. Bio-Medicus ventricular assistance [Editorial]. Ann Thorac Surg 1991;52:180–1.
16. Joyce LD, Kiser JC, Eales F, King RM, Toninato CJ, Hansen J. Experience with the Sarns centrifugal pump as a ventricular assist device. ASAIO Trans 1990;36:M619–23.
17. Ballantyne CM, Verani MS, Short HD, Hyatt C, Noon GP. Delayed recovery of severely "stunned" myocardium with the support of a left ventricular assist device after coronary artery bypass graft surgery. J Am Coll Cardiol 1987;10:710–2.
18. Braunwald E, Kloner RA. The stunned myocardium–prolonged postischemic ventricular dysfunction. Circulation 1982;66:1146–9.
19. Miller CA, Pae WE, Pierce WS. Combined registry for the clinical use of mechanical ventricular assist devices: postcardiotomy cardiogenic shock. ASAIO Trans 1990;36:43–6.
20. Young JN, Iverson IG, Ennix CL, Ecker RR, May IA. Biventricular support is superior to univentricular support for mechanical circulatory assistance in patients after cardiotomy. J Heart Transplant 1987;6:313–4.
21. Pennington DG, Reedy JE, Swartz MT, et al. Univentricular versus biventricular assist device support. J Heart Transplant 1991;10:258–63.
22. Pennock JL, Pierce WS, Wisman CB, Bull AP, Waldhausen JA. Survival and complications following ventricular assist pumping for cardiogenic shock. Ann Surg 1983;198:469–78.
23. Pae WE, Pierce WS, Pennock JL, Campbell DB, Waldhausen JA. Long-term results of ventricular assist pumping in postcardiotomy cardiogenic shock. J Thorac Cardiovasc Surg 1987;93:434–41.
24. Kanter KR, Ruzevich SA, Pennington DG, McBride LR, Swartz MT, Willman VL. Follow-up of survivors of mechanical circulatory support. J Thorac Cardiovasc Surg 1988;96:72–80.
25. Ruzevich SA, Kanter KR, Pennington DG, Swartz MT, McBride LR, Termuhlen DF. Long-term follow-up of survivors of postcardiotomy circulatory support. ASAIO Trans 1988;34:116.
26. Pennington DG, Bernhard WF, Golding LR, Berger RL, Khuri SF, Watson JT. Long-term follow-up of postcardiotomy patients with profound cardiogenic shock treated with ventricular assist devices. Circulation 1985;72(Suppl 2):216–26.
27. Curtis JJ, Walls JT, Schmaltz RA, Boley T, Landreneau R, Nawarawong W. Prognosis of hospital survivors after salvage from cardiopulmonary bypass with centrifugal cardiac assist. ASAIO Trans 1990;36:M552–4.

DISCUSSION

DR O. H. FRAZIER (Houston, TX): I appreciate the opportunity to review this important paper. This group, particularly Dr Golding, has contributed much to our knowledge of using continuous-flow assist devices to treat patients with left ventricular failure. This is a difficult problem we are seeing with increasing frequency.

Although Dr Golding did not comment on his experience with continuous-flow assisted circulation in children, my colleagues and I have had good results in our younger patients with both the Hemopump and the Bio-Medicus pump. This approach has worked particularly well in children with acute allograft rejection, allowing survival of patients who would otherwise have died.

As for which approach to use, we have occasionally found it difficult to cannulate the right superior pulmonary vein in redo procedures. In our experience, cannulation through the aorta can be helpful in such cases. Dr Golding, what alternative methods of cannulation have you used?

Dr DeBakey reported using an LVAD in high-risk patients in the 1960s, and 2 of his patients were long-term survivors. One of the important lessons from that experience, which was also emphasized in this presentation and the one before it, is early use of LVAD support. Even though the device that DeBakey used was crude by today's standards, it played an important role in the survival of these patients. In fact, the device was hooked up preoperatively in high-risk patients. This experience further emphasizes that it is not so much the device but the timing of intervention that allows survival.

We have had some problems in balancing right and left ventricular flow in our patients with BVADs. How does your group balance flow?

I noticed that the use of heparin was discussed in this report. We do not like to use heparin, at least until the bleeding has become inaudible. Heparinization is a tremendous problem in these patients and seems to contribute to the bleeding. In our recent experience with the covalently bonded, heparinized pump, we have not used heparin at all. Dr Golding, what are your thoughts on this topic and on your experience in children?

DR GOLDING: Our involvement with children has been limited. In fact, in this series there were only 3 children, all of whom had undergone a Norwood procedure and were in difficulty. One of them survived to hospital discharge. We have not had experience with pediatric heart transplantation.

Ideally, cannulation involves the left atrium and ascending aorta. However, other options are available. In fact, this series goes back to when I was using a transvalvular aortic valve cannula through a bifurcation graft anastomosed to the ascending aorta. It is a variant of what was described many years ago. Occasionally an apical cannulation technique can work.

One of the objectives is to try to avoid further myocardial injury. However, on occasion, we have put a couple of buttress sutures, made a little stab wound, and slipped the cannula through the apex. That is feasible with continuous-flow devices where the cannulas are much smaller.

Balancing the BVADs can be done only one way—by someone sitting there and using appropriate hemodynamic monitoring. The aim is to try to stabilize all the values, keep the left atrial pressure lower than 15 mm Hg, and try to keep the right atrial pressure lower than 15 mm Hg. Monitoring hemodynamics is the only way to balance these devices.

As Dr Frazier said, heparin cannot be used until you can hear yourself above the noise of the bleeding. Our record on bleeding is not exactly exemplary. We do not use heparin until the bleeding has stopped, and in general, that takes about 24 hours. I endorse the use of the covalently bonded tubing now available, and I think it can diminish the use of heparin. However, I am still nervous about the thought of running these devices without some heparin. Usually we run the activated clotting time at about one and a half times normal and then increase the amount of heparin during the weaning process.

DR JACK J. CURTIS (Columbia, MO): I congratulate Dr Golding and associates on a very well presented and candid report about some dismal survival statistics. At the University of Missouri in Columbia, we have had experience with 91 centrifugal pumps in 67 patients. Although we have used exclusively the Sarns centrifugal pump, our results mirror those just presented. We have also used centrifugal assist for postcardiotomy failure in 54 patients. When left ventricular assist alone was required, we have had a hospital survival rate of 30%. However, when biventricular assist was required, as was the case in 28 patients, only 4 patients survived. This is the same disappointing 14% survival rate Dr Golding described. We have had almost the same complication rates for bleeding and renal failure as The Cleveland Clinic group.

We have been unable to predict in retrospective analysis any determinants of survival, and this seems to be the case across the United States. Importantly, we have never had a survivor who required biventricular assist for greater than 72 hours. All our survivors, however, are in functional class II or I. I wonder as you reflect on this experience, Dr Golding, what you think the cost/benefit ratio is for the 14% who survive. All are very grateful patients who do quite well.

DR GOLDING: You have brought up the unanswerable question that is worrying us all more and more as the pressures get worse in terms of looking at the cost/benefit, not just the risk/benefit, but the cost/benefit ratio. Trying to determine prognostic signs becomes important. Certainly treating these patients is not an inexpensive undertaking, and it also ties up beds in the intensive care unit. For whatever reason, we are not doing as well as some other groups on biventricular support; it is being used very infrequently in our institution. As you mentioned, most of the patients who do well seem to do well fairly quickly and are off the device in about 72 hours. Patients maintained for much longer than that just do not seem to make it.

Again, we need a test that will tell us which patients will do well and which will not. Previously we used to believe that if a patient sustained an infarct in the first 24 hours postoperatively, that was going to be the final straw. Now, at least based on this series, we can no longer say that.

Device-Supported Myocardial Revascularization: Safe Help for Sick Hearts

Michael S. Sweeney, MD, and O. H. Frazier, MD

Department of Thoracic and Cardiovascular Surgery, University of Texas Medical School and The Hermann Hospital, Houston, Texas

Although advances in both the technology of artificial oxygenation and our understanding of myocardial preservation have made aortocoronary bypass operations safer, clinical settings remain where even these improvements have limited efficacy. We have recently treated 43 severely ill patients with aortocoronary bypass, using a ventricular assist device for intraoperative hemodynamic support and ventricular decompression. For 34 of the patients, preoperative ejection fractions (multigated acquisition) ranged from 0.12 to 0.28 (average, 0.22); 6 patients manifested cardiogenic shock preoperatively, and emergency operations precluded multigated acquisition studies. Twenty-nine patients had preoperative evidence of congestive heart failure, 10 had a prior bypass operation, 9 had major chronic obstructive pulmonary disease, and 2 were Jehovah's Witnesses. The operative technique involved minimal doses of heparin (1 to 1.5 mg/kg), no cardioplegia, and no cardiopulmonary bypass. Revascularization was accomplished on beating, nonworking hearts, with right (40 of 43) and left (43 of 43) ventricles supported by Nimbus Hemopumps (4 of 43) or Bio-Medicus centrifugal ventricular assist devices for an average of 112 minutes. In each case, the patient's lungs were used as the oxygenator. An average of 3.7 bypass grafts per patient were constructed. The left internal mammary artery was used in 41 patients, whereas at least one coronary endarterectomy was required in 20. Six patients had concomitant placement of an automatic implantable cardioverter defibrillator. Two patients (4.6%) died: 1 (with preoperative cardiogenic shock) of low cardiac output on postoperative day 1, and 1 of a severe neurologic deficit on day 8. Follow-up ranged from 2 to 18 months (average, 8.9 months), with all survivors demonstrating improvement in cardiac function in both the early and late postoperative periods. We believe that the use of ventricular assist device support for myocardial revascularization has real efficacy, especially in the management of severely ill, high-risk patients at increased operative risk. Moreover, we are encouraged that in selected cases, avoiding pump oxygenation and cardioplegia-induced global ischemic arrest may be a safe strategy.

(Ann Thorac Surg 1992;54:1065–70)

Improvements in artificial oxygenation and in cardiac muscle protection have made aortocoronary bypass (ACB) operations safe for many patients [1–3]. Aortocoronary bypass operations are so safe, in fact, that cardiovascular surgeons may increasingly become victims of their own successes. Presently, more patients at higher than normal risk are considered for ACB [4–7]. Such patients include those who have very poor heart function or congestive heart failure, and those who need an urgent operation after a serious heart attack or a failed balloon angioplasty procedure.

We have recently treated 43 severely ill patients with ACB, using left and, when necessary, right ventricular assist devices (VADs) for intraoperative hemodynamic support and ventricular decompression. Pump oxygenators, cardiac arrest, cardioplegia, and hypothermia were all purposefully avoided. Although patients were operated on for different reasons, their presentations were representative of the spectrum of severely diseased hearts and increased operative risk [5–7]. This unorthodox strategy has produced surprisingly good results to date, and we are encouraged that, in selected cases, savings of both lives and money seem possible.

Patients and Methods

Patients

Between March 1, 1990, and November 30, 1991, 431 patients underwent ACB operations at The Hermann Hospital in Houston, Texas. Of these patients, 43 (10%) were severely ill and required a VAD-assisted ACB operation. In this group, there were 27 men and 16 women, with an average age of 59 years. This subgroup of patients has been identified as being at increased risk for ACB operation [5–7]. For this retrospective study, we reviewed hospital records and follow-up clinic charts of these 43 patients.

For 34 of the 43 patients, preoperative left ventricular ejection fractions were determined through gated blood pool studies, and ranged from 0.12 to 0.28 (average, 0.22). Left ventricular function was quantitated by left ventriculography in 3 other patients. We did not formally measure left ventricular function in 6 patients because they mani-

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Sweeney, Department of Thoracic and Cardiovascular Surgery, University of Texas Medical School, MSMB 1.222, 6431 Fannin, Houston, TX 77030.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

fested cardiogenic shock preoperatively and required emergency ACB. Of the 43 patients, 29 suffered from congestive cardiomyopathy induced by ischemia and were being treated for ventricular failure as well as for coronary artery occlusive disease. In such patients, operation was not undertaken unless the results of thallium stress testing or positron emission tomographic scanning suggested that ischemia was reversible.

In addition, 10 patients had previously undergone an ACB operation, 1 of whom had 2 prior attempts at revascularization. Major chronic obstructive pulmonary disease was present preoperatively in 9 patients and manifested by appropriate symptoms and altered pulmonary function studies (forced expiratory volume in 1 second <60% predicted; forced vital capacity <60% predicted). Each of these patients was being treated medically for pulmonary dysfunction. Two patients who were Jehovah's Witnesses refused to allow transfusion of blood products. Before operation, 9 patients required support by an intraaortic balloon pump.

Operative Technique

After the induction of general anesthesia, a median sternotomy was performed. Heparin was given in only minimal doses (1 to 1.5 mg/kg). Neither cardioplegia nor cardiopulmonary bypass was necessary. Instead, revascularization was accomplished on beating hearts made flaccid by ventricular decompression by temporary VAD support. All 43 patients required support with a left VAD (LVAD). For LVAD support, we used the Hemopump (Johnson & Johnson Interventional Systems, Warren, NJ) (Fig 1) in 4 patients and the Bio-Medicus centrifugal pump (Bio-Medicus, Eden Prairie, MN) in 39 patients. In the 39 patients supported by the Bio-Medicus pump, inflow to the LVAD was accomplished by (1) cannulating the left ventricular apex with a 36F wire-reinforced cannula (Bard Cardiopulmonary Division, Tewksbury, MA) (33 patients) (Fig 2); (2) cannulating the left atrium through the right superior pulmonary vein (3 patients); (3) cannulating the left atrial appendage (1 patient); or (4) cannulating the ascending aorta (2 patients), which was done by advancing the cannula across the aortic valve [8]. In 36 patients, blood was returned from the LVAD to the patient by routine cannulation of the ascending aorta. In 3 patients, blood was returned by cannulating the femoral artery.

Although all patients were supported by the LVAD, we added simultaneous temporary right ventricular support with the Bio-Medicus centrifugal pump to the protocol after the first 3 patients in this series. We found that by decompressing the right ventricle, we could gain optimal exposure of the posterior ventricular and obtuse marginal vessels. Inflow to the right VAD was created by standard right atrial cannulation, whereas right VAD return flow was accomplished by cannulating the main pulmonary artery with a 28F right-angle cannula. Through experience, we have learned that care must be taken to direct the tip of this pulmonary artery cannula into the right pulmonary artery, as the left pulmonary artery proper seems shorter. If the left pulmonary artery is cannulated, the shorter length will cause the cannula tip to wedge in the arterial branches of the upper lobe, resulting in poor oxygenation (Fig 3).

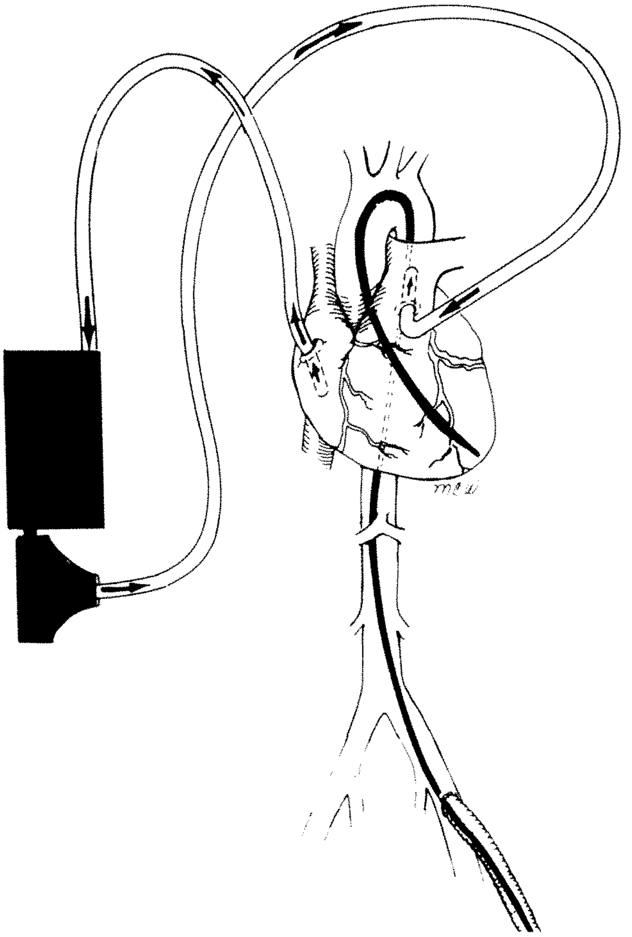


Fig 1. Hemopump left ventricular assist provides for excellent unloading and eliminates the need for two (left-sided) cannulas.

In the last 32 patients, we added high doses of the β-blocking agent esmolol (10 mg/kg intravenous bolus followed by a continuous infusion of 500 $\mu g \cdot kg^{-1} \cdot min^{-1}$) to the preparation. Esmolol, which clears rapidly, lowers vascular resistance and keeps the heart more flaccid. Intraoperative autotransfusion (Cell Saver, Cobe Laboratories, Inc, Lakewood, CA) was used in most patients. The completed operative set-up is shown in Figure 4.

Normothermia was maintained throughout the procedure. The patient's own lungs were used as the oxygenator (100% oxygen delivered through a Siemens Servo 900-C ventilator [Siemens, Siemens-Elena, Sweden]). The myocardium was "protected" by the antegrade flow of the patient's own blood through the coronary arteries. Where distal anastomoses were performed, the vessel being bypassed was temporarily occluded with "lasso" sutures of 5-0 polypropylene placed proximal and distal to the anastomotic site. The esmolol infusion was discontinued when distal anastomoses were completed. Proximal anastomoses were placed in standard fashion on the ascending aorta with the aid of a partially occluding

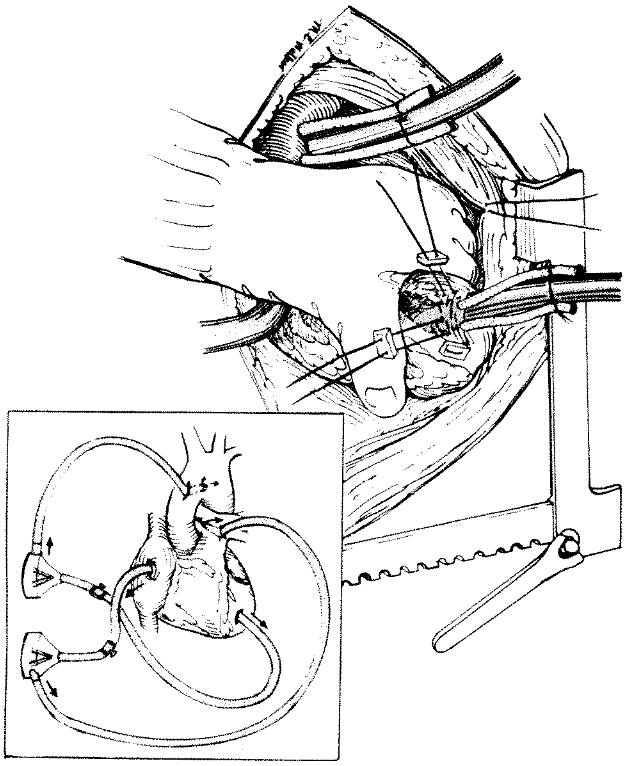


Fig 2. Cannulation of the left ventricular apex for left-side device inflow.

vascular clamp, and patients were weaned from VAD support. Those patients who required extra time in weaning were transported to the intensive care unit (ICU) with the device in place. Heparin was completely reversed in the operating room, even in patients who were transferred to the ICU. We have not found anticoagulation to be necessary during high-flow LVAD support.

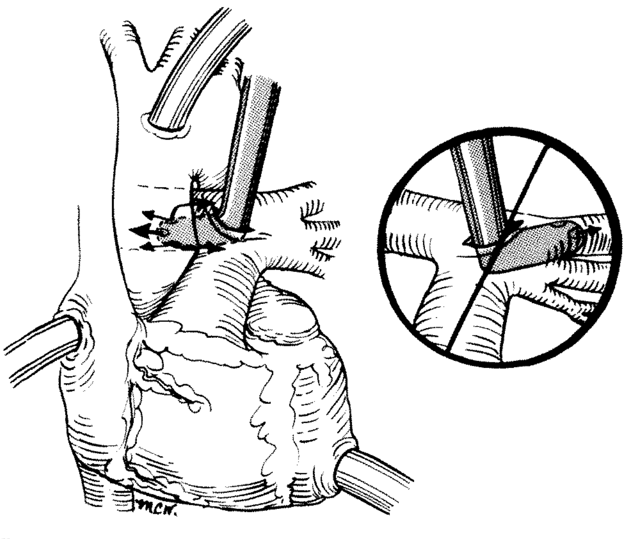


Fig 3. The technique of pulmonary artery cannulation. Patients will not be well oxygenated if the cannula tip is directed into the left pulmonary artery.

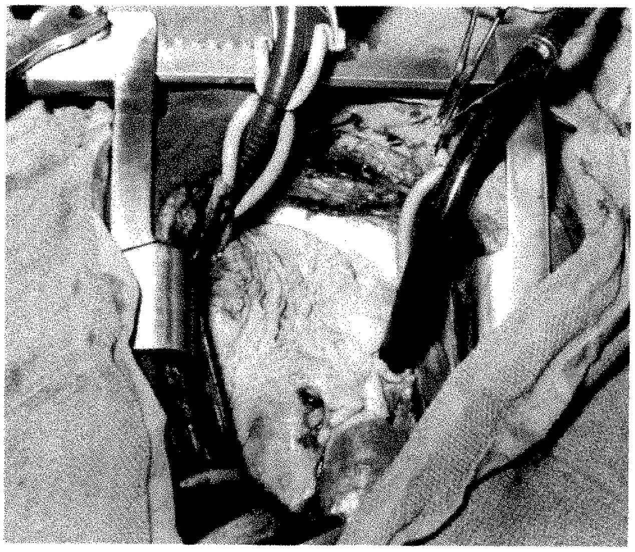


Fig 4. Completed intraoperative set-up when Bio-Medicus pumps are used for right and left ventricular decompression. Note pulmonary and aortic return cannulas at bottom left of photo.

Because of a history of malignant ventricular arrhythmias that were refractory to medical management, 6 patients required concomitant placement of an automatic implantable cardioverter defibrillator (CPI, St. Paul, MN). In 2 patients, carotid endarterectomies were combined with the ACB procedure.

Results

Intraoperative VAD support averaged 112 minutes. All patients were weaned from intraoperative right VAD support. Prolonged LVAD support was needed in 5 patients, who were easily transported to the ICU with the device already in place. Four of these patients were weaned from support. Two patients died. These were the only deaths in our series of 43 patients. One of the deaths occurred in a patient who had preoperative cardiogenic shock. This patient never recovered adequate ventricular function and died of low cardiac output 1 day later. The other patient who died underwent emergency ACB despite a fluctuating neurologic examination. This patient had a marked postoperative neurologic deficit and died on day 8 when support was discontinued.

An average of 3.7 bypass grafts were constructed per patient. In 41 patients, the left internal mammary artery was used as a conduit for at least one distal vessel. Due to the severity of their diffuse coronary atherosclerosis, 20 patients required at least one coronary endarterectomy. Postoperative neurologic problems did not develop in either patient receiving combined ACB and carotid endarterectomy.

Eight patients received thrombolytic therapy in the immediate preoperative period and experienced coagulopathy postoperatively. For the 33 survivors who did not receive thrombolytic therapy, chest tube drainage in the ICU averaged 677 mL (range, 390 to 1,070 mL). In those patients, an average of 0.4 unit of packed red blood cells was transfused (range, 0 to 3 units). For the 41 survivors, the average hospital stay was 10.5 days, with an average of 3.9 of those days being ICU days. For the 33 survivors who did not receive thrombolytic therapy, the average hospital stay was 7.2 days (range, 4 to 21 days), with an average of 1.6 of those days (range, 1 to 3 days) being ICU days.

Follow-up in the 41 survivors ranged from 2 to 21 months (average, 9.4 months). None of the patients have reported angina pectoris, either at rest or with exercise. Of the 29 patients diagnosed preoperatively with congestive cardiomyopathy induced by ischemia, all have reported symptomatic improvement and require either less (20 patients) or no (9 patients) inotropic medication. In 21 of these patients, gated blood pool studies 6 months after operation showed no change (10 patients), some improvement (<10% increase, 8 patients), or much improvement (>10% increase, 3 patients). Ventricular function has not worsened in any of these patients when compared with preoperative status. Follow-up thallium stress testing was available in 29 survivors. These tests showed no change from preoperative status in most (18) patients, improvement in others (11 patients), and worsening in none. Perioperative myocardial infarctions were diagnosed by electrocardiographic findings and serial creatine kinase-MB changes in 2 patients. One of these patients, who had suffered preoperatively from cardiogenic shock, died.

Comment

The benefits of ventricular decompression either in acutely or chronically damaged hearts may be underestimated, especially if such damage is severe. If coronary flow can be maintained or augmented while the ventricular wall tension is markedly reduced, resistance to flow through obstructed coronary arterial beds may be decreased, and, paradoxically, an actual increase in perfusion of ischemic regions of the ventricle seems to occur [9]. Experimentally, Lachterman and associates [10] have used such a model to demonstrate a reduction in the size of an acute infarct when mechanical ventricular decompression is created. These observations are not inconsistent with earlier studies by Buckberg and associates [11, 12] that showed that intramyocardial vessels are constricted in systole by left ventricular wall tension, which causes subendocardial tissues to receive their oxygen during diastole. A reduction in left ventricular wall tension, coupled with augmented coronary flow, should be beneficial for impaired ventricles.

Normothermia and an oxygenated "protection" solution (the patient's own augmented coronary flow) are maintained in this system as well. Randomized clinical studies of antegrade versus retrograde coronary sinus routes for delivery of blood cardioplegia have not demonstrated any advantage of one technique over the other [13, 14]. The experimental advantages of blood cardioplegia have been studied [15, 16], however, and many clinicians employ some form of this protection vehicle [17]. The experimental observation that delivery of blood cardioplegia may be superior to delivery of asanguineous cardioplegia beyond obstructed coronary beds is particularly pertinent [18]. Lichtenstein and associates [19, 20] have recently argued the superiority of warm heart surgery, advocating the maintenance of normothermic temperatures on hearts arrested with warm hyperkalemic blood during aortic cross-clamping. In particular, they have found this method useful in patients with poor ventricular function who require long clamp times, and they believe that the arrested heart continuously perfused with warm blood provides ideal myocardial protection.

Simultaneous left and right ventricular bypass using the patient's lungs as an oxygenator was initially conceived by Drew and associates [21, 22]. Mechanical ventilation of the lungs maintains normal pulmonary metabolism as well as the hemodynamic equilibrium between pulmonary and systemic systems. The transient pulmonary hypertension so often associated with long periods of pulmonary collapse is avoided, and this may foster easy separation from circulatory support. Moreover, prolonged pump oxygenation can theoretically impair subendocardial viability, because all such systems can produce small gaseous and particulate emboli, which travel preferentially to the subendocardium [23]. Although many of our patients had very poor pulmonary function, in no instance were the lungs inadequate as a source of oxygen for the system. In addition, when the patient's lungs become the oxygenator, the cost of extra tubing and equipment is eliminated.

In regard to this method, lengthy debates about reperfusion seem irrelevant. Although the heart continues to beat, it is flaccid, and the distal anastomoses are technically easy to accomplish during several minutes of interrupting flow through the epicardial vessel being bypassed. There were no limitations to fine technical maneuvers routinely employed in operating on arrested hearts, as evidenced by the extensive use of coronary endarterectomy and the almost uniform use of internal mammary arteries as bypass conduits. Two of our patients had organized clots in the region of the left ventricular apex. In this situation, we avoided problems by using the ascending aorta for both inflow and outflow to the LVAD (Fig 5). Whether or not we have actually eluded postcardiotomy pump failure is unknown. Recent data from The Clinical Registry of Mechanical Ventricular Assist Pumps and Artificial Hearts [24] indicate that most patients needing VAD support after acute heart damage cannot be weaned from their devices, and an even smaller percentage ultimately survive. Perhaps such results were avoided in our 43 patients (most of whom were at high risk for postcardiotomy problems) by intervening earlier and by having supportive measures such as ventricular decompression and good coronary perfusion in place, in most cases, before insults occurred. When necessary, we were able to easily transport patients to the ICU with the device already in place. Although in our experience it was not difficult to maintain postoperative support with the Bio-Medicus device, the Hemopump seems particularly well-suited for this strategy. Besides offering excellent

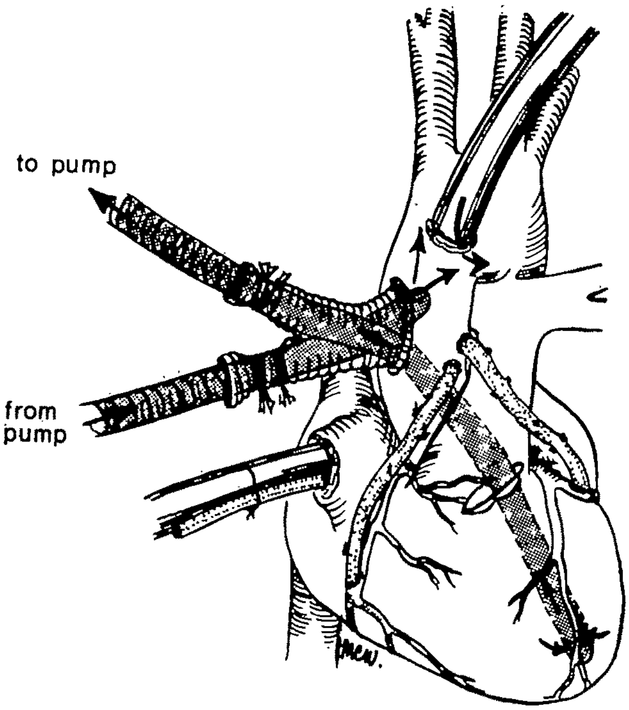


Fig 5. Technique used successfully for left ventricular assist device support on 2 patients with organized thrombus in the left ventricular apex.

intraoperative ventricular decompression, the Hemopump's small size and intravascular placement make it ideally suited for postoperative support.

After operations on the first 4 patients in our series, the Hemopump became unavailable, a result of restrictions imposed by the Food and Drug Administration. However, a new, high-flow model of the Hemopump that should enhance and simplify left ventricular decompression is currently being tested. When approved, this transvalvular device will allow us to use simple aortic root decompression and to avoid left ventricular incisions.

The technique of VAD-supported myocardial revascularization appears to offer several advantages over conventional cardiopulmonary bypass, especially for patients with impaired ventricular function. The lack of aortic cross-clamping avoids global myocardial ischemia, and normothermia preserves normal metabolic processes as well as peripheral perfusion. When the patient's own lungs become the system's oxygenator, cellular and hemodynamic equilibrium is maintained, and expensive equipment is eliminated. Moreover, lower doses of heparin are required, which may potentially reduce the incidence of coagulopathy and the need for transfusion of blood products. Myocardial protection is achieved by coupling mechanical ventricular decompression with the patient's own normal or augmented coronary flow. Thus, expensive cardioplegia delivery systems with their complex hyperkalemic solutions become unnecessary. In addition to maintaining a tranquil operative field, high doses of β-blockers may be beneficial on their own merit [25]. In our system, they are rapidly cleared and, thus, can be used without consequence. If postcardiotomy device support is required, the VADs are already in place and working, allowing for an easy transfer to the ICU. In such cases, improved patient outcomes may be possible, because intervention is early and the heart is maintained in a relaxed, decompressed state with coronary perfusion now improved by operation. This technique may avoid endocardial ischemia, which can occur in already compromised patients who must undergo prolonged attempts at weaning from cardiopulmonary bypass before LVAD support can be instituted. We are encouraged that the technique of VAD-supported revascularization is safe, is probably less expensive than conventional methods, and offers real advantages in the management of critically ill patients.

References

1. CASS principal investigators and their associates. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery, survival data. Circulation 1983;68:939–50.
2. Miller DW, Hessel EA, Winterscheid LC, Merendino KA, Dillard DH. Current practice of coronary artery bypass surgery: results of a national survey. J Thorac Cardiovasc Surg 1977;73:75–83.
3. Cooley DA. Myocardial revascularization: past accomplishments, current trends. J Appl Cardiol 1989;4:357–64.
4. Jones EL, Weintraub WS, Craver JM, Guyton RA, Cohen CL. Coronary bypass surgery: is the operation different today? J Thorac Cardiovasc Surg 1991;101:108–15.
5. Edwards FH, Bellamy RF, Burge JR, et al. True emergency coronary bypass surgery. Ann Thorac Surg 1990;49:603–11.
6. Naunheim KS, Fiore AC, Arango DC, et al. Coronary artery bypass grafting for unstable angina pectoris: risk analysis. Ann Thorac Surg 1989;47:569–74.
7. Naunheim KS, Fiore AC, Fagan DC, et al. Emergency coronary artery bypass grafting for failed angioplasty: risk factors and outcome. Ann Thorac Surg 1989;47:816–22.
8. Duncan JM, Baldwin RT, Igo SR, Frazier OH. Myocardium-sparing cannulation technique for left ventricular assist device support. Ann Thorac Surg 1991;52:565–6.
9. Lachterman BS, Felli P, Amirani J, Pina V, Smalling RW. Improved myocardial blood flow during partial regional ischemia using the Hemopump. Clin Res 1990;38:375A.
10. Lachterman BS, Felli P, Smalling RW, et al. Improved infarct salvage by left ventricular unloading with the Hemopump immediately prior to and during reperfusion after a 2-hour coronary occlusion. J Am Coll Cardiol 1991;17(Suppl 2A):134A.
11. Hoffman JIE, Buckberg GD. In: Yu PN, Goodwin JF, eds. Transmural variation in myocardial perfusion. Progress in Cardiology. Philadelphia: Lea & Febiger, 1976;5:37–89.
12. Brazier J, Cooper N, Buckberg GD. The adequacy of subendocardial oxygen delivery: the interaction of determinants of flow, arterial oxygen content and myocardial oxygen need. Circulation 1974;49:968–77.
13. Diehl JT, Eichhorn EJ, Konstam MA, et al. Efficacy of retrograde coronary sinus cardioplegia in patients undergoing myocardial revascularization: a prospective, randomized trial. Ann Thorac Surg 1988;45:595–602.
14. Fiore AC, Naunheim KS, Kaiser GC, et al. Coronary sinus versus aortic root perfusion with blood cardioplegia in elective myocardial revascularization. Ann Thorac Surg 1989;47:684–8.
15. Follette DM, Mulder DG, Maloney JV Jr, Buckberg GD. Advantages of blood cardioplegia over continuous coronary perfusion and intermittent ischemia—an experimental and clinical study. J Thorac Cardiovasc Surg 1978;76:604–17.

16. Follette DM, Fey K, Becker H, et al. Superiority of blood cardioplegia over asanguinous cardioplegia: an experimental and clinical study. Langenbecks Arch Chir 1980;351:279–83.
17. Barner HB. Blood cardioplegia: a review and comparison with crystalloid cardioplegia. Ann Thorac Surg 1991;52:1354–67.
18. Robertson JM, Buckberg GD, Vinten-Johansen J. Cardioplegic delivery beyond coronary stenosis: the superiority of blood cardioplegia over asanguineous cardioplegia. Surg Forum 1981;32:286–7.
19. Lichtenstein SV, el-Dalati H, Panos A, Slutsky AS. Long cross-clamp with warm heart surgery [Letter]. Lancet 1989;1:1443.
20. Lichtenstein SV, Ashe KA, el-Dalati H, Cusimano RJ, Panos A, Slutsky AS. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
21. Drew CE, Keen G, Benazen DB. Profound hypothermia. Lancet 1959;1:745–7.
22. Drew CE, Anderson IM. Profound hypothermia in cardiac surgery. Lancet 1959;1:748–50.
23. Utley J, Carlson EL, Hoffman JIE, Martinez HM, Buckberg GD. Total and regional myocardial blood flow measurement with 25 micron, 9 micron, and filtered 1–10 micron diameter microspheres and antipyrine in dogs and sheep. Circ Res 1974;34:391–405.
24. Willerson JT, Frazier OH. Reducing mortality in patients with extensive myocardial infarction. N Engl J Med 1991;325:1166–8.
25. Reimer KA, Rasmussen MM, Jennings RB. Reduction by propranolol of myocardial necrosis following temporary coronary occlusion in dogs. Circ Res 1973;33:353–60.

DISCUSSION

DR ROBERT L. KORMOS (Pittsburgh, PA): It is not unusual for us to take for granted the need for cardiopulmonary bypass in order to accomplish cardiac operations. Indeed, many of us may listen to this report and say, why mess with tradition? Recently, however, investigators have recognized that cardiopulmonary bypass has effects on the central nervous system and on renal, hepatic, and pulmonary microvasculature. It results in the activation of multiple inflammatory mediators primarily associated with the use of oxygenators. This novel report by Dr Sweeney and Dr Frazier is particularly important as it presents an approach to cardiac surgery that attempts to reduce these negative effects of bypass, especially in this critically ill group of patients with decreased left ventricular function. I would like to ask Dr Sweeney the following questions.

First of all, do you plan to carry out studies in future patients that would substantiate your claims that hearts supported in this fashion have more normal perfusion and metabolism? Second, in our own group of 28 patients supported by a left ventricular assist device as a bridge to cardiac transplantation, only 25% required additional right ventricular support for concomitant right ventricular failure. Therefore, do you propose to simplify your methods by using left ventricular bypass alone, and if so, will you have a method of selecting patients who will need both left ventricular and right ventricular bypass? Finally, can you determine whether it was your surgical approach and techniques or your methods of circulatory support alone that led to your excellent results in this group of patients with depressed left ventricular function? In other words, do you plan a randomized trial comparing this method and traditional methods of cardiopulmonary bypass?

I would like to thank The Society for the privilege of discussing this exciting report, and Drs Sweeney and Frazier for the opportunity to review the manuscript. I would also like to congratulate the authors for their vision and courage in exploring this method of circulatory support for cardiac surgery.

DR SWEENEY: Thank you for your comments. I will try to answer your questions as quickly as I can. In fact, there were 4 of the 43 patients who required left ventricular device support alone. The Nimbus Hemopump is particularly well-suited for this purpose because it avoids cannulation of the left side of the heart. Unfortunately, the early version of that pump only has flows of about 4 L/min. In patients with acute infarcts who are otherwise healthy, without any element of pulmonary hypertension, that is adequate to decompress the right ventricle as well, and allows the same operation to be performed as would be performed on an arrested heart. With some patients with congestive cardiomyopathy, or those who have had embarrassment of their left ventricular function for a long enough period of time, there is compensation by elevation of the pulmonary vascular resistance and increase in right heart pressures. In such patients, a right ventricular device was added, in particular the Bio-Medicus pump. The Johnson and Johnson Corporation has in fact created a shorter, stiffer version of the Hemopump, which can be inserted in the operating room by the surgeon through a stab in the ascending aorta. This pump can be passed quickly and easily across the aortic valve, generating flow rates between 7 and 10 L/min in our laboratory. Those flow rates seem adequate to decompress the right ventricle as well. It seems attractive to think that only one cannulation site would be required, and that transportation to the intensive care unit with the device in place would be facilitated.

Whether or not we have avoided postcardiotomy pump problems in this group of patients is really unknown to us. It is just conjecture. The most recent updates from the combined registry of device-supported patients were presented at an interim meeting of this Society in San Francisco not long ago, and they continue to demonstrate that, after a decade of experience in the group of patients who are postcardiotomy pump failures alone, the sad fact is that most of the patients cannot be weaned from device support, and in those who are weaned, most of them are not long-term survivors. Our study group of patients is different in this regard, and we are encouraged that perhaps the earlier intervention and ease in transport to the intensive care unit has allowed a more favorable outcome.

Early Cellular Events in the Lung Allograft

Riad Adoumie, MD, Cyril Serrick, BS, Adel Giaid, PhD, and Hani Shennib, MD

The Joint Marseille-Montreal Lung Transplant Program, Montreal, Quebec, Canada

We hypothesized that ischemic insult to the lung allograft may render it more susceptible to rejection. Left canine single-lung allografts were subjected to usual periods of cold and warm ischemia (4 hours and 1 hour, respectively). Bronchoalveolar lavage and open lung biopsies were performed at 0, 1, 4, and 24 hours and 1 week after transplantation. Bronchoalveolar lavage fluid was examined for cellular phenotypes, lymphocyte lectin-mediated cytotoxicity, and natural killer cell cytotoxicity. Open lung biopsy specimens were examined for severity of injury/rejection and MHC class II expression. Within 1 to 4 hours of reimplantation, we observed marked influx of polymorphonuclear leukocytes and lymphocytes and an increase in lectin-mediated cytotoxicity (25.6% ± 14.8% and 50.6% ± 20.1% versus 5.4% ± 7.5% preoperatively; $p < 0.05$). In addition, natural killer cell cytotoxicity increased from 10.2% ± 13.5% before transplantation to 20.5% ± 8.6% 4 hours after transplantation ($p < 0.03$). By 24 hours MHC class II expression became evident and continued to increase while subtle histologic evidence of rejection appeared by 1 week. We conclude that ischemia-reperfusion injury can alter the local bronchopulmonary milieu, thus rendering it more susceptible to the development of rejection.

(Ann Thorac Surg 1992;54:1071–7)

Despite its increasing applicability, lung transplantation continues to be plagued by numerous challenging problems. In the early postoperative period lung dysfunction remains common. This is usually attributed to ischemia-reperfusion injury, atelectasis, rejection, or infection.

Advances in lung preservation techniques have greatly reduced the incidence of early graft dysfunction. These techniques, however, remain largely empirical. Cellular events in the lung allograft after ischemia and reperfusion remain poorly understood. Insult to the lung during the process of harvesting, subsequent ischemia, and implantation can induce an inflammatory response that might affect not only the short-term function of the allograft but also its long-term outcome.

Bronchoalveolar lavage (BAL) has gained popularity as a valuable method to study cellular events in the lung and to aid in the diagnosis of various lung pathologies [1, 2]. Using this technique Shennib and associates [3–5] were able to demonstrate specific alterations in the phenotype of cells harvested from the bronchoalveolar space in the setting of infection, atelectasis, or rejection. Similarly, Chang and colleagues [6] have recently demonstrated early elevation in BAL levels of interleukin-2 (IL-2), γ-interferon (IFN-γ), and tumor necrosis factor α (TNF-α) in the setting of rejection and suggested that these could be used as early markers for rejection.

There is ample evidence that nonallogenic stimuli such as viral infections might predispose an allograft to rejection [7–11]. Although the mechanism for this remains unclear, it has been suggested that infection might result in the local release of certain cytokines including IL-2 and IFN-γ, which are capable of upregulating MHC class II expression, thus rendering the allograft more immunogenic. Recent evidence by Yang and Welsh [12] seems to suggest that such stimuli might also lead to activation of alloreactive cytotoxic T cells, which might in turn lead to injury of the graft.

In the absence of an ideal method of lung preservation, we continue to observe evidence of mild ischemia-reperfusion injury in almost all our patients. In most cases this remains short-lived, however. Acute rejection seems also to occur rather frequently and at an early stage, usually by the second week after transplantation. We hypothesized that ischemic-reperfusion injury to the lung allograft might lead to alterations in the immune cellular and humoral milieu within the lung allograft that render it more vulnerable to the development of early acute rejection.

In this study, we simulated the clinical setting of lung transplantation by performing single-lung transplantation between conditioned, nonrelated dogs. Allografts were subjected to 4 hours of cold ischemia and 1 hour of warm ischemia. Recipients received immunosuppressive medications similar to those used in patients. Early cellular changes in the bronchopulmonary compartment of the lung allograft were studied.

Material and Methods

Sixteen size-matched mongrel dogs (weight, 20 to 25 kg) were subjected to left single-lung allotransplantation. All animals were handled and cared for in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH publication No. 85-23, revised 1985). The donor heart and lungs were harvested en bloc after the pulmonary artery was flushed with 2 L of modified Euro-Collins solution

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Shennib, The Joint Marseille-Montreal Lung Transplant Program, Montreal General Hospital, 1650 Cedar Ave, Montreal, Que, Canada H3G 1A4.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

(Euro-Collins + 3 mEq/L sodium bicarbonate + 12.8 mEq/L magnesium sulfate) [13]. The block was then stored in an ice box at 4°C for 4 hours in an inflated state. Immediately before implantation, the left lung was separated from the block and the hilar structures were prepared for anastomosis. Left lung allotransplantation was performed using a standard technique described by Veith and Richards [14]. Warm ischemia time was carefully maintained at 1 hour when the hilar clamps were removed.

Immunosuppression

Cyclosporine, 30 mg/kg, was given orally preoperatively followed by 17 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ given in divided doses starting the first postoperative day. Administration of azathioprine at a dose of 2 mg/kg was started preoperatively and continued daily. Methylprednisolone, 10 mg/kg intravenously, was given before reperfusion and followed by 5 mg/kg intravenously every 8 hours for 3 doses; thereafter, prednisone, 20 mg, was given orally once a day.

Bronchoalveolar Lavage

Multiple aliquots of 30 to 40 mL of normal saline solution were instilled through a polyethylene tube wedged into the specific segment and then gently aspirated. Lavage was performed from different lung regions each time to avoid a direct effect of repeat BAL on cellular composition [15]. Furthermore the animals were divided into two groups. In group 1, BAL was performed at 4 hours and 1 week after transplantation. In group 2, BAL was performed at 1 and 24 hours after reimplantation. Preoperative baseline levels were obtained by lavaging the donor right lower lobe before lung retrieval.

Cell Preparation

BRONCHOALVEOLAR LAVAGE LYMPHOCYTES. The BAL fluid was filtered through two layers of cotton gauze to remove clumps of mucus. The cells were then collected by centrifugation at 1,500 rpm for 10 minutes. The BAL cells were washed in RPMI-1640 enriched with 10% fetal calf serum, penicillin (100 IU/mL), streptomycin (100 μg/mL) and glutamine (2 mmol/L) (RPMI-complete). Total cell counts were performed using an improved Neubaeuer hemocytometer using 1% acetic acid as the counting fluid. Bronchoalveolar lavage cell viability was routinely assessed using the Trypan blue exclusion test and was normally at more than 90%. Slide preparations were made in a cytocentrifuge using 100 μL of BAL cell suspension at 5×10^6 cells/mL and by spinning at 500 rpm for 5 minutes. Differential cell counts were made using a leukostat stain kit (Fisher Scientific, Orangeburg, NY) for a total of 400 cells. Bronchoalveolar lavage cells were then enriched for lymphocytes using the nylon wool column technique. Lymphocytes were then adjusted to appropriate concentrations for cytotoxic assays.

PERIPHERAL BLOOD MONONUCLEAR CELLS. Heparinized peripheral blood samples were obtained at the same time as BAL. Peripheral blood lymphocytes were isolated using the Ficoll-Hypaque discontinuous gradient technique. The cells were then washed using RPMI-complete and adjusted to appropriate concentrations for the cytotoxic assay.

Cytotoxic Assays

NATURAL KILLER ASSAY. The cytotoxic function of natural killer (NK) cells was measured using a previously described technique [4, 16]. In summary, 10^4 canine thyroid adenocarcinoma target cells were incubated with 100 μL of effector lymphocytes at effector to target ratios of 50:1, 25:1, and 12.5:1 using a round-bottom 96-well tissue culture plate. Assays were done in triplicate. The culture plates were incubated at 37°C in 5% CO_2 for 6 hours, then centrifuged at 1,500 rpm for 5 minutes. One hundred microliters of supernatant was harvested, and radioactivity was quantitated in a gamma scintillation counter. Percentage cytotoxicity was measured using a standard formula:

$$\text{Percentage cytotoxicity} = \frac{\text{CPM Experimental} - \text{CPM Spontaneous}}{\text{CPM Total} - \text{CPM Spontaneous}} \times 100,$$

where CPM = counts per minute; CPM Spontaneous = spontaneous release as determined from wells containing target cells and medium alone; and CPM Total = total release as determined by incubating target cells with 100 μL of 0.5% Triton × 100. Spontaneous release was usually less than 10%.

LECTIN-DEPENDENT CELL-MEDIATED CYTOTOXICITY. This assay is regarded as a quantitative measurement of the total cell-mediated cytotoxicity of a T cell population and has previously been described [17–19]. In summary, the assay was conducted in a similar fashion to the one described above using Raji cells as targets. In addition, concanavalin A is added to the culture medium at a concentration of 8 μg/mL. Spontaneous release was usually less than 20%.

Histology

Open lung biopsies were performed before BAL by wedging out a small fragment of the lung. Specimens were fixed in Bouin's solution for 6 hours at room temperature. Tissues were then washed several times with 30% ethanol and processed in paraffin. Sections of 4-μm thickness were cut from several levels of each block and mounted on glass slides. Conventional histologic examination was done using hematoxylin and eosin. Immunohistochemistry was performed using the avidin-biotin-peroxidase method. In brief, sections were dewaxed in xylene, dehydrated in decreasing concentrations of ethanol, washed in 0.1 mol/L phosphate-buffered 0.15 mol/L saline solution (PBS), and incubated in PBS containing 0.3% hydrogen peroxide to block endogenous peroxidase activity. They were then washed in PBS, incubated in 10% normal horse serum, and then incubated with BIF6, a monoclonal antibody to canine MHC class II antigen (a gift from Dr R. Alejandro) [20], for 16 hours at 4°C. After three 5-minute washes in PBS, sections were incubated with the second layer antibody, biotinylated horse anti-mouse immunoglobulin G (Vector Labs), at a dilution of 1/200 for 45 minutes at room temperature. This was followed by three 5-minute washes in PBS and further incubation with the avidin-biotin-peroxidase complex (Vectastain Elite Kit; Vector Labs) at a dilution of 1/200 for 45 minutes at room temperature. The immunoreaction was visualized by developing sections of 0.025% 3,3′ diaminobenzidine and 0.03% hydrogen peroxide for 5 minutes at room temperature. Sections were then washed in distilled water, stained with hematoxylin, dehydrated in ethanol, cleared in xylene, and mounted in tissue mount. Negative control sections were immunostained in the absence of the first or second layer antiserum. Positive control sections were immunostained with antiserum to Von Willebrand factor (factor VIII-related antigen). The immunostaining grading system was adapted from Chang and colleagues [6]: 0 = weak or no staining similar to negative control samples; 1 = distinct focal staining for MHC, class II; 2 = multifocal intense staining; and 3 = intense staining throughout the tissue cells.

Statistical Analysis

Results are presented as mean ± standard deviation. The paired Student's *t* test was used to compare repeated measurements from the same animal. Values of p less than 0.05 were considered statistically significant.

Results

Single-lung transplantations were performed between 16 pairs of animals. Of a total of 16 recipients studied, heartworm infection led to exclusion of 2. Four other animals that received transplants were excluded due to development of atrial thrombosis or pneumonia. Thus, 10 dogs were effectively included in the study, 5 in each of groups 1 and 2.

Bronchoalveolar Lavage and Peripheral Blood Lymphocyte Phenotypes and Function

Shortly after reperfusion we observed an increase in the number of cells retrieved from the bronchoalveolar compartment. At 1 and 4 hours, this was 34.5 ± 19.9 × 10^4 and 35.0 ± 13.7 × 10^4 cells/mL, respectively, compared with a preoperative control value of 23.7 ± 14.9 × 10^4 cells/mL. This increase reached its peak at 24 hours (42.9 ± 14.9 × 10^4 cells/mL) ($p < 0.06$). At 1 week, the number of cells retrieved decreased but remained higher than preoperative values (36.8 ± 13.8 × 10^4 cells/mL). As expected, the polymorphonuclear leukocytes accounted for the bulk of this cellular influx. At 1 hour, the percentage of polymorphonuclear lymphocytes in the BAL fluid was 27.4% ± 21.8% compared with a preoperative control value of 7.1% ± 6.5%. Influx of polymorphonuclear lymphocytes peaked at 4 hours (49.6% ± 16.0%; $p = 0.015$) and remained significantly higher than the preoperative value at 24 hours (37.4% ± 21.9%; $p < 0.05$). At 1 week, the percentage of polymorphonuclear leukocytes in the BAL fluid decreased but remained higher than the preoperative value (19.0% ± 14.3%).

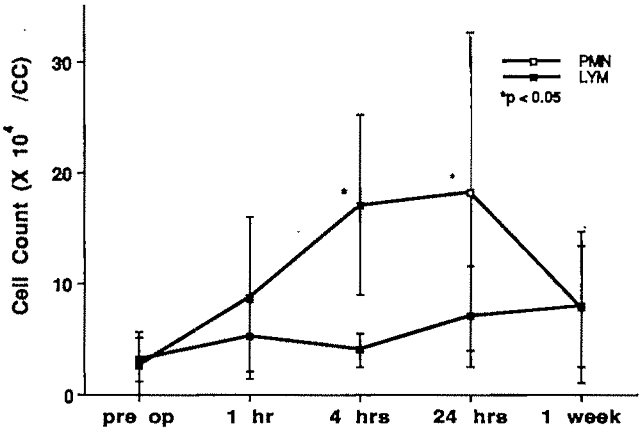


Fig 1. Total cell count (10^4/mL) of polymorphonuclear leukocytes (PMN) and lymphocytes (LYM) obtained in bronchoalveolar lavage.

In addition to neutrophil influx, we observed a progressive increase in the number of lymphocytes in the BAL fluid. At 1 and 4 hours, this was 5.2 ± 3.1 × 10^4 and 4.0 ± 1.5 × 10^4 cells/mL versus a preoperative control value of 3.1 ± 1.9 × 10^4 cells/mL. At 24 hours, this increased to 7.0 ± 4.5 × 10^4 cells/mL, and it reached its highest value at 1 week (7.9 ± 5.5 × 10^4 cells/mL) (Fig 1).

Lectin-dependent cell-mediated cytotoxicity of BAL lymphocytes showed a significant increase 1 and 4 hours after implantation (before transplantation, 5.4% ± 7.5%; after 1 hour, 25.6% ± 14.8% [$p < 0.02$]; 4 hours, 50.6% ± 20.1% [$p < 0.03$]). At 24 hours, this decreased to 8.2% ± 6.6%, and it remained low at 1 week (12.4% ± 8.4%). In contrast, no significant change was detectable in lectin-dependent cell-mediated cytotoxicity in peripheral blood lymphocytes. At 1 and 4 hours, this was 1.0% ± 2.0% and 9.3% ± 16.4% compared with a control pretransplantation value of 0.4% ± 1.1%. At 24 hours and 1 week, peripheral lectin-dependent cell-mediated cytotoxicity remained low at 1.1% ± 2.3% and 1.2% ± 1.6%, respectively (Fig 2).

Natural killer cell cytotoxicity was similar to the pre-

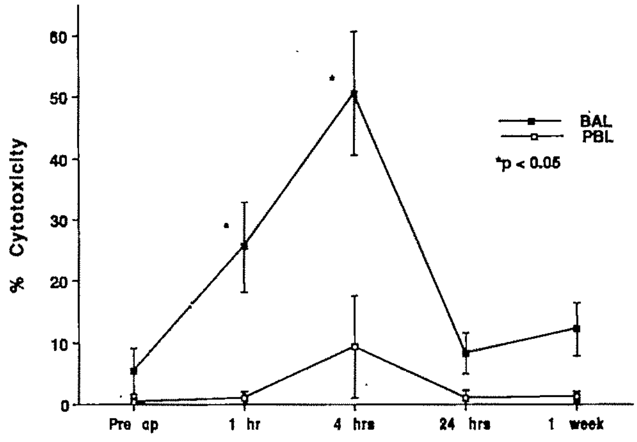


Fig 2. Lectin-dependent cell-mediated cytotoxicity in bronchoalveolar lavage fluid (BAL) and peripheral blood (PBL). Results are shown at an effector to target ratio of 50:1.

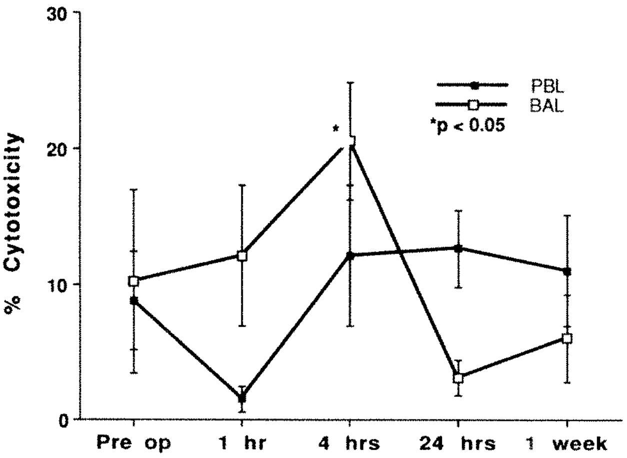


Fig 3. Natural killer cell cytotoxicity in bronchoalveolar lavage fluid (BAL) and peripheral blood (PBL). Results are shown at an effector to target ratio of 50:1.

transplantation value at 1 hour (before transplantation, 10.2% ± 13.5%; 1 hour, 12.1% ± 10.4%); however, it increased significantly by 4 hours after transplantation (20.5% ± 8.6%; $p < 0.03$). By 24 hours, NK cytotoxicity seemed to rapidly decrease, and it remained below control values at 1 week (3.1% ± 2.6% and 6.0% ± 6.4% respectively). In contrast, peripheral blood NK cytotoxicity showed no significant change. At 1 and 4 hours, this was 1.5% ± 1.8% and 12.1% ± 10.4%, respectively, versus a pretransplantation value of 8.8% ± 7.2%. This remained unchanged from the pretransplantation value at 24 hours and 1 week, with percentage cytotoxicity at 12.6% ± 5.6% and 11.0% ± 9.1%, respectively (Fig 3).

Histology

As expected, on the hematoxylin and eosin stain, there was evidence of an inflammatory response by 1 hour after reperfusion, with neutrophil margination and areas of alveolar edema. These changes were more pronounced at 4 hours, with areas of neutrophil infiltration into parenchyma and alveolar spaces. This inflammatory response was persistent at 24 hours. In 4 of 5 biopsy specimens studied at 1 week, there was evidence of grade 1 or 2 rejection with perivascular lymphocyte cuffing. This was evident despite maintenance of triple immunosuppression (Fig 4).

Immunohistochemical staining of preoperative specimens showed no evidence of MHC class II expression on either bronchial or vascular tissue. By 24 hours, we observed focal staining in the peribronchial tissue of lung allografts. At 1 week, however, there was evidence of more diffuse and intense staining in the peribronchial tissue. Similarly, we detected increased staining in the perivascular and peribronchial mononuclear cellular infiltrate at 1 week. The endothelium, on the other hand, remained negative (Table 1; see Fig 4).

Comment

There is evidence that nonspecific stimuli such as viral infections might predispose an allograft to rejection both by rendering it more immunogenic through the release of a variety of cytokines and through activation and recruitment of alloreactive T cells capable of initiating a rejection response [7, 8, 12]. We have recently shown that a standard ischemic insult similar to the one used in this study is capable of inducing local production of cytokines IL-2, TNF-α, and IFN-γ in the lung allograft (Serrick C, Shennib H, Adoumie R; unpublished results). Such mediators might play an important role in initiating the early inflammatory changes and the increased T lymphocyte and NK cell cytotoxicity seen in this study. Furthermore, such mediators are also known to be important regulators of MHC antigen expression and of allograft immunogenicity. Thus, the early inflammatory response might set the stage for acute rejection demonstrated as early as 1 week after transplantation.

In the absence of immunosuppression, the lung allograft should proceed to severe rejection with progressive increase in T cell and NK cell cytotoxicity [5] together with an increase in IL-2, TNF-α, and IFN-γ levels in the lung allograft [6]. The observation that all these parameters return to low levels and remain depressed at 1 week is probably a reflection of the effect of immunosuppressive medications (cyclosporine, azathioprine, and steroids) and the short-lived nature of ischemia-reperfusion injury.

The role of lymphocytes in modulating ischemic lung injury remains unclear. Traditionally, it has been suggested that neutrophils seem to mediate the bulk of vascular and parenchymal damage after an acute inflammatory stimulus to the lung. Recent evidence seems to indicate that NK- and IL-2–activated lymphocytes might exert a cytotoxic effect on lung vascular endothelium [21, 22]. Using an endotoxin-treated sheep model, Meyrick and Brigham [23] have also been able to demonstrate preferential sequestration and activation of lymphocytes within 20 to 45 minutes of endotoxin infusion. In this study, we demonstrated that an ischemic insult of comparable magnitude to what is frequently experienced clinically results in early lymphocyte sequestration and activation and increased T lymphocytes and NK cell cytotoxicity. Such influx of cytotoxic lymphocytes might therefore contribute to lung allograft injury and dysfunction seen after reimplantation.

Previous work from this laboratory and that by others have suggested that elevation of BAL lectin-dependent cell-mediated cytotoxicity could be used as an indicator of early development of rejection. In this study, we have failed to see such an increase despite histologic evidence of rejection in some animals at 1 week. In previous work cyclosporine tapering or withdrawal was used to initiate acute rejection. In this study, animals were maintained on the same daily maintenance doses of cyclosporine, azathioprine, and steroids. Thus, the increased T lymphocyte cytotoxicity might be attributable to a different mechanism of rejection in the absence of cyclosporine or to the fact that more advanced stages of rejection were previously being described.

In this study, we have observed that activation of lymphocytes in response to ischemia was confined to the

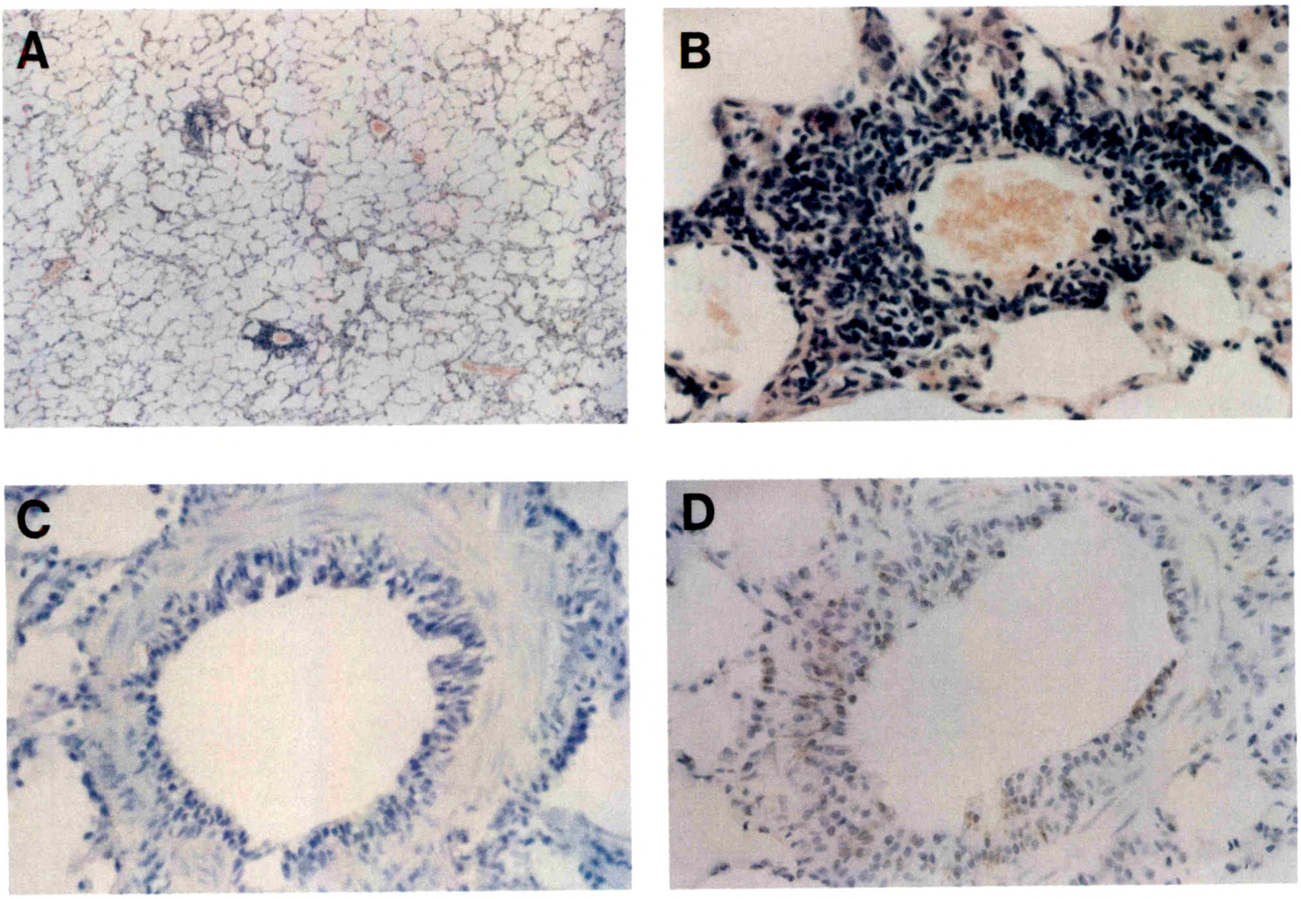


Fig 4. (A and B) Perivascular mononuclear infiltrate in lung allograft biopsy specimen at 1 week after transplantation (hematoxylin and eosin; A ×60, B ×360, both before 7% reduction). (C and D) Canine lung allograft at 1 week after transplantation (C) immunostained in the absence of MHC class II antiserum and (D) immunostained with MHC class II antiserum, both with hematoxylin counterstain (both ×240 before 7% reduction).

bronchopulmonary compartment, as lymphocytes isolated simultaneously from the peripheral blood failed to show similar activation. These findings probably reflect the selective recruitment of effector cells into the allograft in response to the nonspecific ischemic or allogenic stimulus and support the use of BAL rather than blood sampling as a more sensitive tool to study cellular events in the lung allograft. We are currently studying the effects of ischemia or reperfusion in an autoimplanted lung model to dissect further whether the observed changes seen early and late after lung ischemia are totally nonspecific or modulated in part by an allogenic stimulus.

Table 1. Grading of MHC Class II Antigen Expression[a]

Time	Bronchial Epithelium	Vascular Endothelium	Cellular Infiltrate
Preop	0	0	0–1
1 hour	0	0	0–1
4 hours	0	0	0–1
24 hours	0–1	0	0–1
1 week	1–2	0	1–2

[a] MHC class II expression on the allograft bronchial epithelium and vascular endothelium and the mononuclear perivascular and peribronchial infiltrate. Grade 0 = weak or no staining similar to negative control; grade 1 = distinct focal staining; grade 2 = multifocal intense staining; and grade 3 = intense staining throughout the tissue cells.

In this animal model, expression of MHC class II antigens on bronchial epithelium but not vascular endothelium is rather interesting. Using a rat model, Romaniuk and associates [11] also demonstrated that in the setting of rejection, MHC class II antigens were induced on bronchial tissue only. Recent work by Chang and colleagues [6] using a canine model has suggested that MHC class II antigens were equally expressed over bronchial epithelium as well as vascular endothelium when rejection was induced by withholding cyclosporine. Such a discrepancy between our results and those of Chang and colleagues might again represent a difference in severity or mechanism of rejection in the absence of cyclosporine. Alternatively, these findings might reflect the higher vulnerability of bronchial epithelium to ischemic insults, particularly given that our method of preservation involves administering Euro-Collins solution through the pulmonary artery and that until recently we have focused most of our evaluation of methods of preservation on lung parenchymal function but not airway integrity.

One limitation inherent in the canine model used in this study is the heterogeneity of the animals used. This choice was dictated by the lack of a reproducible small animal model for lung transplantation. In fact, this heterogeneity may have accounted for the relatively large standard deviation in results and the variability in severity of rejection observed at 1 week.

We conclude that our standard technique of lung preservation and immunosuppression fails to abrogate the inflammatory effects of ischemia. Such inflammatory insult contributes to the local influx and activation of immune effector cells such as cytotoxic T cells and NK cells with the release of mediators such as IFN-γ, TNF-α, and IL-2. These not only might contribute to early graft dysfunction but might predispose it later to rejection through upregulation of its MHC class II antigen expression. The use of monoclonal antibodies directed against IL-2, TNF-α, and IFN-γ might be useful in improving current methods of lung preservation.

Supported in part by a grant from the Canadian Cystic Fibrosis Foundation, the Quebec Heart Foundation, and the Quebec Lung Association. Dr Shennib is a recipient of a scholarship from the "Fonds de la Recherche en Santé du Québec."

References

1. Reynolds HY. Bronchoalveolar lavage. Am Rev Respir Dis 1987;135:250-3.
2. Shennib H, Nguyen D. Bronchoalveolar lavage in lung transplantation. Ann Thorac Surg 1991;51:335-40.
3. Shennib H, Nguyen D, Guttman RD, Mulder DS. Phenotypic expression of bronchoalveolar lavage cells in lung rejection and infection. Ann Thorac Surg 1991;51:630-5.
4. Nguyen DM, Mulder DS, Shennib H. Altered cellular immune function in the atelectatic lung. Ann Thorac Surg 1991;51:76-80.
5. Nguyen DM, Mulder DS, Shennib H. Lymphocytic cytotoxicity in rejecting and infected lung allografts. Transplantation (in press).
6. Chang SC, Hsu HK, Perng RP, Shiao GM, Lin CY. Increased expression of MHC class II antigens in rejecting canine lung allografts. Transplantation 1990;49:1158-63.
7. Burke CM, Glanville AR, Theodore J, Robin ED. Lung immunogenicity, rejection and obliterative bronchiolitis. Chest 1987;92:547-9.
8. Allen MD, Burke CM, McGregor GA, Baldwin JC, Jamieson SW, Theodore J. Steroid responsive bronchiolitis after human heart-lung transplantation. J Thorac Cardiovasc Surg 1986;92:449-51.
9. Hall BM, Duggin GG, Philips J, Bishop GA, Horvath JS, Tiller OJ. Increased expression of HLA-DR antigens on renal tubular cells in renal transplants: relevance to the rejection response. Lancet 1984;2:247-51.
10. Halloran PF, Wodgymar A, Autenried P. The regulation of expression of major histocompatibility complex products. Transplantation 1986;41:413-20.
11. Romaniuk A, Prop J, Arjen HP, Wildevuur CRH, Nieuwenhuis P. Expression of class II major histocompatibility complex antigens by bronchial epithelium in rat lung allografts. Transplantation 1987;44:209-14.
12. Yang H, Welsh RM. Induction of alloreactive cytotoxic T cells by acute virus infection of mice. J Immunol 1986;136:1186-93.
13. Jamieson SW, Stinson EB, Oyer PE, Baldwin JC, Shumway NE. Operative technique for heart and lung transplantation. J Thorac Cardiovasc Surg 1984;87:930-5.
14. Veith FJ, Richards K. Improved technique for canine lung transplantation. Ann Surg 1970;171:553-8.
15. Cohen AB, Bactra GK. Bronchoscopy and lung lavage induced bilateral neutrophil influx and blood leukocytosis in dogs and monkeys. Am Rev Respir Dis 1980;122:239-42.
16. Loughran TP Jr, Joachim DH, Storb R. Morphologic and phenotypic analysis of canine natural killer cells: evidence of T-cell lineage. Cell Immunol 1985;95:207-17.
17. Emeson EE, Norin AJ, Veith FJ. Lectin dependent cell-mediated cytotoxicity. A new and simple method to quantitate cytotoxic T cell activity in dogs. Transplantation 1982;33:365-72.
18. Bonavida B, Bradley TP. Studies on the induction and expression of T cell mediated immunity versus lectin-induced nonspecific cell mediated cytotoxicity by alloimmune lymphocytes. Transplantation 1976;21:94-102.
19. Bevan MJ, Cohn M. Cytotoxic effect of antigen and mitogen induced T cells on various targets. J Immunol 1975;114:559-67.
20. Alejandro R, Shienvold FL, Latif Z, Esquenazi V, Miller J, Mintz DH. Monoclonal antibodies recognizing canine and human Ia like antigens. Transplantation 1984;38:542-3.
21. Newman JH. Lung vascular injury. Chest 1988;93:3:139-45.
22. Duke S, King L, Jones M, Newman J, Brigham K, Forbes S. Human recombinant interleukin-2 activated sheep lymphocytes: sheep pulmonary vascular epithelial cells. Physiologist 1987;30:173-3.
23. Meyrick B, Brigham KL. Acute effects of *Escherichia coli* endotoxin on the pulmonary microcirculation of anesthetized sheep: structure-function relationships. Lab Invest 1983;48:458-70.

DISCUSSION

DR CRAIG R. SMITH (New York, NY): I enjoyed this thought-provoking study from a group that is making a lot of contributions in this area. I do not disagree with your conclusions, but I am not sure you have addressed the hypothesis. Although it is a beautiful description of early events after transplantation, it is purely descriptive and does not establish a connection between ischemic injury and rejection. I assume this is a preliminary step toward models that will allow you to isolate ischemic injury from rejection.

In a more clinical vein, do you know of any evidence in lung, liver, or any other solid organ of a connection between ischemic time, for example, and either the severity or frequency of early rejection? Along similar lines, has anyone shown a connection between ischemic time and the production of donor-specific antiHLA antibody directed against class II determinants?

DR ADOUMIE: To answer the first part of your question, the hypothesis was to test whether ischemia predisposes the lung to rejection. In this study, we have established that after ischemia there are changes in the lung allograft that have been previously suggested to predispose an allograft to rejection. Shortly thereafter a high incidence of rejection is observed. This is descriptive as you have suggested. Having established that, our next step would be indeed to try to correlate the severity of ischemic changes with the grade of rejection.

As for the second part, I am not aware of any conclusive clinical evidence to establish a relationship between ischemic injury and rejection. It would be interesting to review the large experience accumulated with renal allografts. But considering how good the quality of both renal preservation and clinical outcome are, this will probably be difficult to establish.

DR AXEL HAVERICH (Hannover, Germany): Dr Adoumie, I very much enjoyed your report. I think an important question is being raised, because we are all concerned about long ischemic times in clinical lung transplant programs. In our own experience with more than 70 lung transplants now, however, we have failed to correlate the ischemic time with long-term pulmonary function testing. Also, like Dr Smith, I think you should include groups with different times of ischemia to separate the effects described. In addition, don't you think it would be a good idea to include an autotransplantation model in your series to separate the ischemic changes from those precipitated from rejection?

DR ADOUMIE: Thank you, Dr Haverich, for sharing your observations in a large series of lung transplants. In this study, the end points we have used are perhaps more sensitive than the ones you used in your clinical observations. Having established the changes we found after ischemia, the next step would be to create a variable ischemic time among different groups as you and Dr Smith have suggested. An autotransplantation model currently undertaken would help determine whether this response is alloantigen-dependent or nonspecific. I suspect that lymphocyte activation and increased major histocompatibility antigen expression occur in a nonspecific fashion after ischemia. These changes would not predispose the autotransplant to rejection because it shares the same antigens with the host.

Bioassay of EDRF From Internal Mammary Arteries: Implications for Early and Late Bypass Graft Patency

Paul J. Pearson, MD, PhD, Paulo R. B. Evora, MD, PhD, and Hartzell V. Schaff, MD

Cardiac Surgical Research and Section of Cardiovascular Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

To study the basal, luminal release of endothelium-derived relaxing factor, 35-mm segments of canine internal mammary artery (IMA) were cannulated and perfused at 5 mL/min in vitro with physiological salt solution. Vasoactive properties of the effluent were bioassayed on coronary artery smooth muscle. Effluent from IMAs produced significant vasodilation of the bioassay ring compared with effluent from a prosthetic conduit (n = 24; $p < 0.05$). The vasodilation by the effluent could be eliminated by mechanically removing the intima of the IMA, or by treating the IMA segments with N^G-monomethyl-L-arginine or N^G-nitro-L-arginine, two competitive inhibitors of nitric oxide synthesis from L-arginine; vasodilation was not influenced by treatment with indomethacin. In 83% of the superfusion experiments, effluent from the left IMA induced greater relaxation of the bioassay ring than did effluent from the right IMA. In addition, the average vasodilation induced by left IMA effluent was 28% ± 2.3% versus 17.4% ± 3.1% for the right (n = 24; $p < 0.05$). However, in organ chamber experiments, right and left IMAs exhibited comparable endothelium-dependent vasodilation to acetylcholine (n = 6). Because endothelium-derived relaxing factor induces vasodilation and also inhibits platelet adhesion, platelet aggregation, and atherogenesis, luminal release of endothelium-derived relaxing factor by the IMA could contribute to superior results when the artery is used in bypass grafting.

(Ann Thorac Surg 1992;54:1078–84)

Physiology of the internal mammary artery (IMA) has come under intense investigation because of excellent late patency when this vessel is used as a conduit for coronary artery bypass [1]. Luscher and colleagues [2] have postulated that patency of IMA coronary artery bypass grafts is maintained because of enhanced production of endothelium-derived relaxing factor (EDRF). The active component of EDRF is the nitric oxide radical [3, 4], which is also the active component of nitrovasodilators such as sodium nitroprusside and nitroglycerin [5]. Enhanced production of EDRF by IMA grafts would serve to act as the coronary bypass graft's own endogenous nitrovasodilator [6].

Endothelium-derived relaxing factor is released bidirectionally by the endothelium. Extraluminal release of EDRF acts on the adjacent vascular smooth muscle to promote vasodilation [2]. Release of EDRF into the lumen of the vessel would inhibit platelet aggregation [7] and adhesion [8], and promote platelet disaggregation in the graft [7]. In addition, intraluminally released EDRF could travel to "downstream" arterial beds to promote vasodilation [9].

Previous experiments studying the physiological responses of the IMA have used organ bath experiments in which the release of EDRF is studied by examining its effect on the underlying vascular smooth muscle (extraluminal release) [2]. Such organ chamber studies cannot detect or quantify the release of EDRF into the lumen of the vessel. In the present experiments, we designed a bioassay apparatus to detect luminal release of EDRF from canine IMAs.

Material and Methods

Harvesting of Tissue

Heartworm-free mongrel dogs (25 to 30 kg) of either sex were anesthetized with intravenous pentobarbital sodium (30 mg/kg bolus injection; Fort Dodge Laboratories, Fort Dodge, IA) and exsanguinated; the right and left IMAs were dissected free from the chest wall, and the beating heart was excised and immersed in cool, oxygenated physiological salt solution of the following millimolar composition: NaCl, 118.3; KCl, 4.7; $MgSO_4$, 1.2; KH_2PO_4, 1.22; $CaCl_2$, 2.5; $NaHCO_3$, 25.0; and glucose, 11.1 (control solution). The procedures and the handling of the animals were reviewed and approved by the Institutional Animal Care and Use Committee of the Mayo Foundation.

In Vitro Experiments

The left circumflex coronary artery was carefully dissected free from the heart and placed in control solution. The left circumflex coronary artery and both right and left IMAs were then cleaned of connective tissue, and particular care was taken not to touch the intimal surface of the blood vessels.

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Schaff, Section of Cardiovascular Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Organ Chamber Experiments

Rings of right and left IMA (5 to 6 mm in length) were prepared from each artery. In rings in which vascular smooth muscle function was to be examined without the influence of the endothelium, the intima was removed by gentle rubbing of the intimal surface with the tip of a pair of watchmakers' forceps [10]. Previous histological studies have shown that this procedure successfully removes the endothelial cells in large canine arteries while preserving the ability of the vascular smooth muscle to contract and relax.

The rings were suspended in 25-mL organ chambers filled with control solution maintained at 37°C and aerated with 95% O_2 and 5% CO_2 (pH = 7.4) [10]. Each ring was suspended by two stainless steel clips passed through the lumen. One clip was anchored to the bottom of the organ chamber; the other was connected to a strain gauge (Statham Gould UC2) for the measurement of isometric force. Rings were placed at the optimal point of their length–tension relationship by progressively stretching them until the contraction to KCl (20 mmol/L), imposed at each level of distention, was maximal [10, 11]. In all experiments, the presence or absence of endothelium was confirmed by the response to acetylcholine (10^{-6} mol/L) of rings contracted with potassium ions (20 mmol/L) [10, 11]. After optimal tension was achieved, the rings were allowed to equilibrate for 45 minutes before the administration of drugs.

Bioassay Experiments

The bioassay apparatus is shown in Figure 1. In this system, the biological activity of EDRF released from the IMA (approximately 5 cm long, right or left) was bioassayed by a coronary ring (proximal left circumflex coronary artery) from which the endothelium had been removed mechanically [12]. The IMAs were perfused at a constant flow (5 mL · min^{-1}) with control solution aerated at 37°C. There was a transient delay of 1 second before the fluid reached the bioassay rings, which were suspended below the donor segment. The tension developed in the rings was recorded. The bioassay rings were first superfused for 60 minutes with control solution, which passed through a stainless steel cannula (direct superfusion). During this time, coronary artery rings were stretched in a stepwise fashion to their optimal tension (10 g). Control perfusion was provided from an aerated tower. An adjacent aerated tower contained control solution plus prostaglandin $F_{2\alpha}$ (2×10^{-6} mol/L).

Relaxation response of the bioassay rings was examined during a contraction caused by prostaglandin $F_{2\alpha}$. The absence of endothelium on the bioassay ring was confirmed by the lack of relaxation to acetylcholine (10^{-7} mol/L) infused under direct superfusion. The bioassay ring could also be superfused with solution pumped through the IMAs (endothelial superfusion). In some experiments, the endothelium in the IMAs was removed by rubbing the intimal surface with a small stainless steel probe. The effectiveness of endothelium removal was confirmed by a lack of EDRF release from the IMA segment (evidenced by relaxation of the coronary artery bioassay ring) by infusion of acetylcholine (10^{-7} mol/L) in the perfusion fluid.

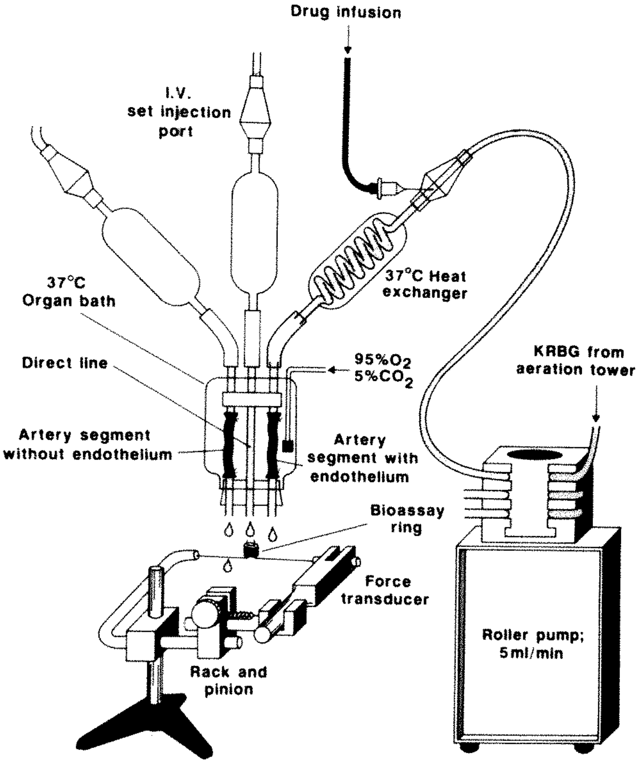


Fig 1. Bioassay apparatus for the measurement of luminal endothelium-derived relaxing factor production from perfused arterial segments. (I.V. = intravenous.)

In 19 of the bioassay experiments, the right and left IMA segments were preserved in formalin. After perfusion experiments, IMA segments were incised longitudinally to expose the intimal surfaces. The blood vessels were then mounted on specimen cards and photographed beside a pathologist's measuring card. Eight by 10-inch enlargements of the photographs were obtained, and the surface areas of the segments were measured using computer-assisted planimetry. By calibrating the computer with the measuring card in the photograph, we calculated absolute surface area of the right and left IMA segments.

Drugs

The following drugs were used: acetylcholine chloride, indomethacin, norepinephrine, prostaglandin $F_{2\alpha}$, and sodium nitroprusside (all from the Sigma Chemical Company, St. Louis, MO). L-arginine, N^G-nitro-L-arginine, and N^G-monomethyl-L-arginine were obtained from Calbiochem, San Diego, CA. All drugs were prepared daily with distilled water except for indomethacin, which was dissolved in Na_2CO_3 (10^{-5} mol/L). Oxyhemoglobin was prepared using the method of Gillespie and Sheng [13]. The concentrations are expressed as final molar concentration in the organ chamber. When N^G-nitro-L-arginine, N^G-monomethyl-L-arginine, or hemoglobin was used, vascular segments were exposed to the compound at least 15 minutes before experimentation. When indomethacin

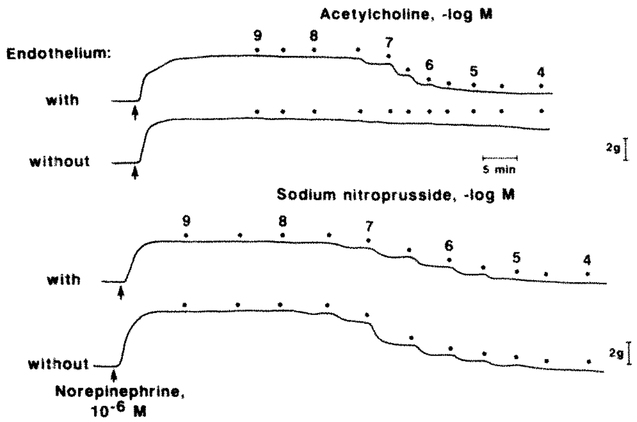


Fig 2. Endothelium-dependent (acetylcholine) and endothelium-independent (sodium nitroprusside) relaxation of canine internal mammary arteries (original trace). Segments of left internal mammary artery (with and without endothelium) were suspended in organ chambers and contracted with norepinephrine. After the contraction to norepinephrine was stable, the arteries were exposed to increasing concentrations of acetylcholine or sodium nitroprusside.

Table 1. Values for 50% Inhibition of Right and Left Internal Mammary Arteries With and Without Endothelium[a]

Group	Left IMA	Right IMA
With endothelium		
Acetylcholine	7.00 ± 0.09	7.19 ± 0.06
Acetylcholine + indomethacin	7.06 ± 0.15	6.74 ± 0.21
Sodium nitroprusside	6.75 ± 0.13	6.97 ± 0.18
Without endothelium		
Sodium nitroprusside	7.03 ± 0.09	7.25 ± 0.08

[a] Values are shown as the negative logarithm of the effective molar concentration of the agonist causing 50% inhibition of contraction to norepinephrine.

IMA = internal mammary artery.

(10^{-5} mol/L) was used to prevent synthesis of endogenous prostanoids, the tissue was treated with the compound at least 40 minutes before experimentation.

Data Analysis

The results are expressed as means ± the standard error of the mean. In all experiments, n refers to the number of animals from which rings or bioassay segments were taken. In rings contracted with norepinephrine, responses are expressed as percent changes from contracted levels. For relaxations, the negative logarithm of the effective molar concentration of the agonist causing 50% inhibition of contraction to norepinephrine was calculated for the concentration–response curves, and the mean of these values is presented. For bioassay experiments, relaxations are expressed as percent change in tension from the contraction of the bioassay ring to prostaglandin $F_{2\alpha}$. For relaxations, the negative logarithm of the effective molar concentration of agonist causing 50% inhibition (IC_{50}) of the contractions to prostaglandin $F_{2\alpha}$ was calculated for concentration–response curves, and the mean of these values is presented. Statistical evaluation of the data was performed by Student's *t* test for either paired or unpaired observations. Values were considered to be significantly different when *p* was less than 0.05.

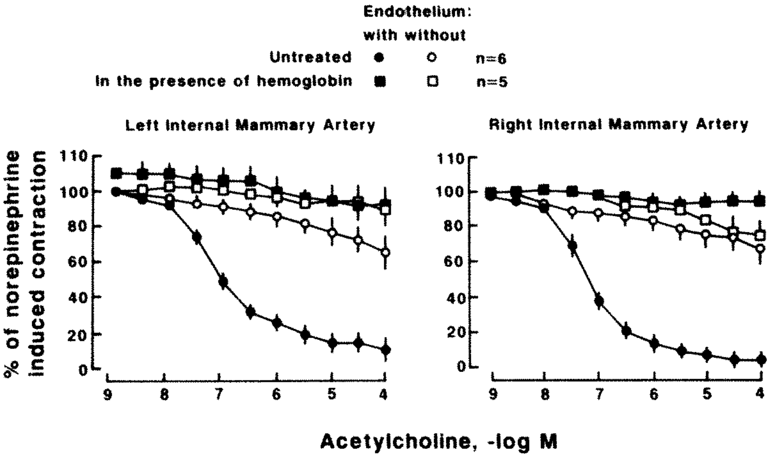
Results

Organ Chamber Studies

ENDOTHELIUM-DEPENDENT RELAXATION. In IMA segments that had been contracted with norepinephrine (10^{-6} mol/L), acetylcholine (10^{-9} to 10^{-4} mol/L) caused concentration-dependent relaxation of right and left arterial segments with endothelium but no change in tension in arterial segments without endothelium (Figs 2, 3). The endothelium-dependent vasodilation to acetylcholine was comparable in the right and left IMA (Table 1). Acetylcholine-mediated endothelium-dependent vasodilation in right and left IMAs could be inhibited by hemoglobin (10^{-5} mol/L) or by pretreatment with N^G-monomethyl-L-arginine (10^{-4} mol/L) (Figs 3, 4). Indomethacin (10^{-5} mol/L) had no effect on endothelium-dependent relaxation to acetylcholine (Fig 4; see Table 1).

ENDOTHELIUM-INDEPENDENT RELAXATION. In arterial segments precontracted with norepinephrine, sodium nitroprusside (10^{-9} to 10^{-4} mol/L) caused concentration-dependent relaxation of right and left IMAs (Fig 5; see Fig

Fig 3. Concentration–response curves to acetylcholine (10^{-9} to 10^{-4} mol/L) in right and left canine internal mammary arteries. Values are presented as means ± standard error of the mean and represent change in tension from the initial contraction to norepinephrine (100%). Hemoglobin was used at a concentration of 10^{-5} mol/L. (Untreated = control response.)



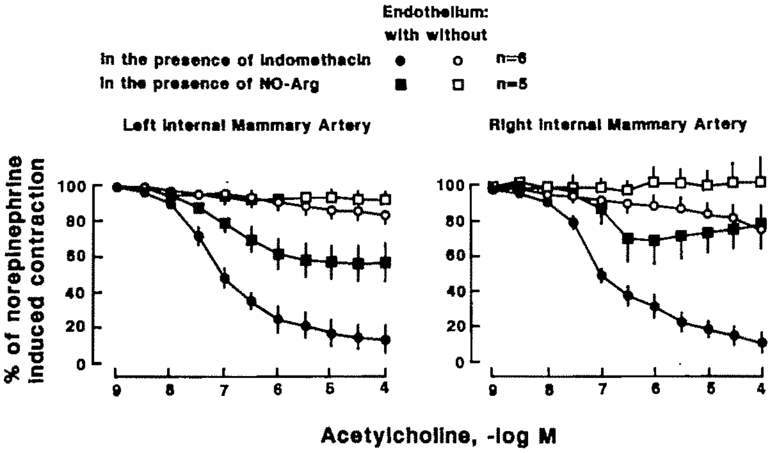


Fig 4. Concentration–response curves to acetylcholine (10^{-9} to 10^{-4} mol/L) in right and left canine internal mammary arteries. Values are presented as means ± standard error of the mean and represent change in tension from the initial contraction to norepinephrine (100%). Indomethacin was used at a concentration of 10^{-5} mol/L and N^G-nitro-L-arginine (NO-Arg) at a concentration of 10^{-4} mol/L.

2). There was no significant difference between arteries with and without endothelium in response to sodium nitroprusside, and there was no difference between the reactivity of the right versus the left IMA to the agonist (see Table 1).

Bioassay Experiments

After the coronary artery bioassay ring had been contracted by the addition of prostaglandin $F_{2\alpha}$ (2×10^{-6} mol/L) to the perfusate, switching of the perfusate from the stainless steel cannula (direct superfusion) to either the right or left IMA (endothelial superfusion) caused a stable relaxation of the bioassay ring indicating the basal release of EDRF by the IMA (Fig 6). The relaxation induced by superfusion through the IMAs could be prevented by mechanical removal of the endothelium in the conduit, by the addition of *N*^{G}-monomethyl-L-arginine (10^{-4} mol/L) or *N*^{G}-nitro-L-arginine (10^{-4} mol/L) to the perfusion fluid (Fig 7; see Fig 6). The addition of indomethacin (10^{-5} mol/L) to the perfusion fluid had no effect on the relaxant activity of the effluent from either the right or left IMAs (see Figs 6, 7).

In 20 of 24 superfusion experiments (83%), the left IMA exhibited greater luminal release of EDRF than the right IMA as evidenced by greater relaxation of the coronary artery bioassay ring by effluent from the perfused arteries (Fig 8). In addition, the average vasodilation of the coronary artery bioassay ring induced by effluent from the left IMA was 28.9% ± 2.3% versus 17.4% ± 3.1% for the right ($p < 0.05$) (see Fig 8). The enhanced relaxation induced by the left versus the right IMA was independent of the order of the superfusion (ie, which vessel was superfused first), and there was no significant difference in the level of precontraction of the bioassay ring before left versus right IMA superfusion. In addition, when measured using computer-assisted planimetry, the average surface area of the right versus the left IMA in 19 consecutive studies was 251.1 ± 8.9 and 251.6 ± 9.0 mm^2, respectively.

Comment

The major findings of this experiment were: (1) the right and left IMA exhibit comparable extraluminal release of EDRF to acetylcholine and comparable vasodilation to sodium nitroprusside; (2) the right and left IMA exhibit significant intraluminal release of EDRF, which induced relaxation of coronary arterial smooth muscle; and (3) the left IMA has a significantly greater luminal release of EDRF than the right IMA.

Enhanced release of EDRF by arterial conduits may explain, in part, the superior late patency compared with veins when these vessels are used as arterial bypass grafts [2]. The active component of EDRF is the nitric oxide radical [3, 4], which also accounts for the vasodilatory action of currently used nitrovasodilators [5]. In the endothelial cell, nitric oxide is synthesized from the amino acid L-arginine [14], and nitric oxide synthesis can be inhibited by substituted derivatives of L-arginine such as *N*^{G}-monomethyl-L-arginine and *N*^{G}-nitro-L-arginine [15,

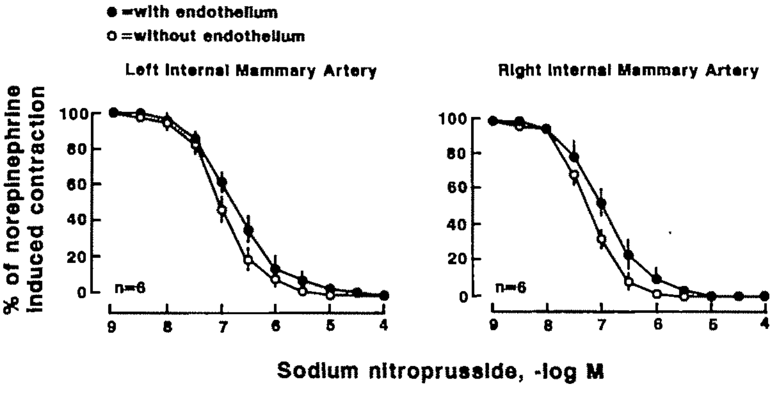


Fig 5. Concentration–response curves to sodium nitroprusside (10^{-9} to 10^{-4} mol/L) in right and left canine internal mammary arteries. Values are presented as means ± standard error of the mean and represent change in tension from the initial contraction to norepinephrine (100%).

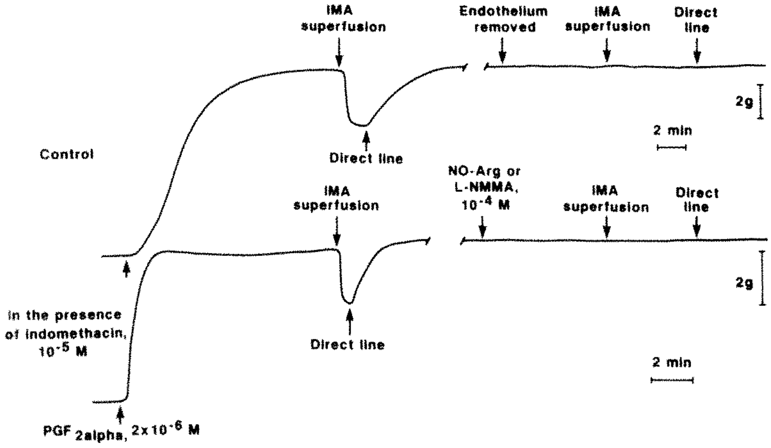


Fig 6. Bioassay of endothelium-derived relaxing factor (EDRF) from canine left internal mammary arteries (IMAs) (original trace). Arterial segments were perfused at 5 mL · min^{-1} with control solution. When the coronary artery bioassay ring was exposed to prostaglandin $F_{2\alpha}$ (PGF$_{2alpha}$) through the prosthetic conduit (direct line)*, it exhibited contraction (top trace). However, when the perfusion fluid was switched so as to pass through the IMA segment with endothelium* (IMA superfusion)*, the coronary artery relaxed, indicating a basal release of EDRF. When the perfusion fluid was again switched back to the direct line, the bioassay ring again regained constriction, indicating the removal of the vasodilator action of EDRF. If the endothelium was mechanically removed from the IMA segment, superfusion through the segment no longer induced relaxation of the coronary artery bioassay ring (top trace). Indomethacin treatment of the IMA did not alter the vasodilator activity of the effluent from the perfused vessel (bottom trace). However, treatment of the IMA with either* N^G*-nitro-L-arginine* (NO-Arg) *or* N^G*-monomethyl-L-arginine* (L-NMMA) *completely abolished the vasodilator activity of the perfused IMA with endothelium (bottom trace).*

16]. Indeed, in the present investigation, release of EDRF in both the organ chamber and bioassay experiments was prevented by these inhibitors.

The finding that the cyclooxygenase blocker indomethacin had no effect on endothelium-dependent vasodilation of the IMA supports the belief that EDRF is not a prostanoid or a product of the cyclooxygenase pathway. The endothelium of the IMA does produce prostacyclin [17–19]. However, apparently the amount of prostacyclin produced by the IMA endothelium under basal conditions is not enough to induce vascular relaxation of epicardial coronary artery smooth muscle. Indeed, compared with EDRF, prostacyclin is a relatively weak epicardial coronary vasodilator [20].

Additional evidence that EDRF from the canine IMA is the nitric oxide radical is provided by our finding that oxyhemoglobin blocks endothelium-dependent vasodilation. Oxyhemoglobin scavenges the nitric oxide radical and is a selective inhibitor of vasodilation due to release of nitric oxide [13, 21]. Further, the present study verifies that all nitric oxide was generated by the intima; removal of the endothelium completely inhibited endothelium-dependent vasodilation in organ chamber and bioassay experiments.

Like prostanoids, EDRF is released bidirectionally by the endothelium; extraluminal EDRF acts on the underlying vascular smooth muscle, and intraluminal EDRF is released into the blood. Early after bypass grafting, extraluminal release of EDRF would promote vasodilation of the graft (Fig 9). Because nitric oxide inhibits mitogenesis and smooth muscle proliferation [22], long-term extraluminal EDRF production might also inhibit atherosclerosis. Previous in vitro studies of IMA graft function have used organ chambers that primarily measure the effect of extraluminally released EDRF during stimulation with various agonists and antagonists [2, 23]. The bioassay

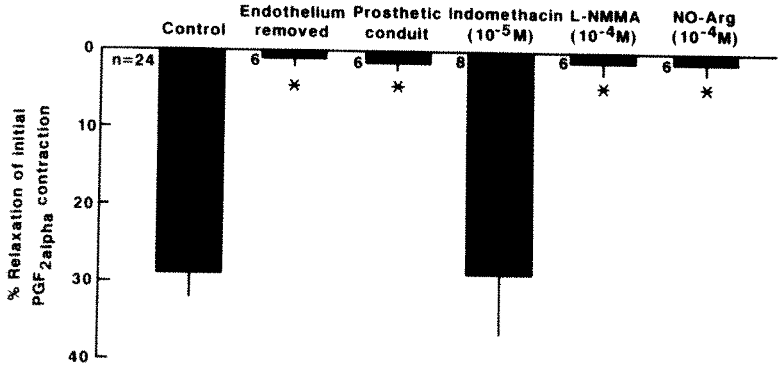


Fig 7. Bioassay of endothelium-derived relaxing factor from perfused canine left internal mammary arteries (IMAs). Values are presented as means ± standard error of the mean and represent percent relaxation of the canine coronary artery bioassay ring which had been contracted with prostaglandin $F_{2\alpha}$ (PGF$_{2alpha}$; 2×10^{-6} mol/L). (Control = *relaxation induced by effluent from perfused IMA;* Endothelium removed = *relaxation induced by IMA that had the intima mechanically removed;* Prosthetic conduit = *relaxation induced in the bioassay ring by perfusion through a stainless steel tube;* Indomethacin, L-NMMA *[*N^G*-monomethyl-L-arginine], and* NO-Arg *[*N^G*-nitro-L-arginine] represent relaxation induced by effluent from the perfused internal mammary artery that had been treated with the respective drugs;* *$p < 0.05$ *versus control relaxation.)*

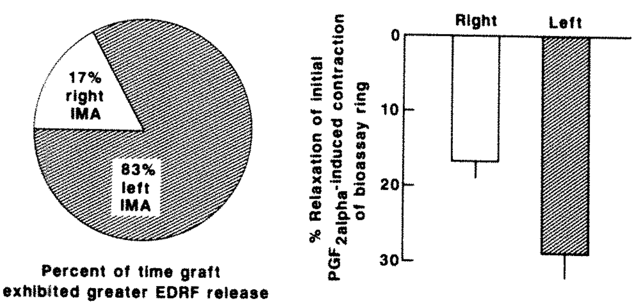


Fig 8. Comparison of endothelium-derived relaxing factor (EDRF) *release from left versus right internal mammary arteries* (IMAs). (PGF_{2alpha} = *prostaglandin* $F_{2\alpha}$.)

system used in this study documents intraluminal release of EDRF from the perfused IMA under basal (unstimulated) conditions.

In the early period after bypass grafting, intraluminal production of EDRF may have several important actions. Intraluminal release of EDRF prevents platelet adhesion to the intima [8]. Because vasospasm is directly related to platelet deposition [24] such an action would serve secondarily to decrease vascular tone. In addition, intraluminally released EDRF inhibits platelet aggregation and promotes platelet disaggregation [7] through a cyclic guanosine monophosphate–dependent mechanism [25]. Finally, intraluminally released EDRF may cause vasodilation of downstream arterial beds (see Fig 9) [9]. Such vasodilator activity was demonstrated in the present experiment by the profound relaxation of the coronary artery bioassay ring by effluent from the perfused IMA segments. Because the luminal release of EDRF is augmented with increasing blood flow [12], this action might be expected to be more pronounced in the high-flow conditions in vivo.

An unexpected finding in the present study was the demonstration that the left IMA releases more EDRF intraluminally than the right IMA. Such a finding cannot be attributed to different sizes of the arteries, as surface areas of the grafts were equal. It is possible that the different embryologic origins of the two arteries account for this finding. The right IMA is derived from the fourth aortic arch on the right side during development [26]. However, the left IMA is not derived from an aortic arch but from the left seventh intersegmental artery [26]. There is heterogeneity in the production of EDRF in human arteries from different locations [27]. In clinical practice, enhanced intraluminal production of EDRF in the left IMA could be a factor, in addition to technical considerations, for the superior long-term patency of the graft for coronary bypass as compared with the right IMA [28].

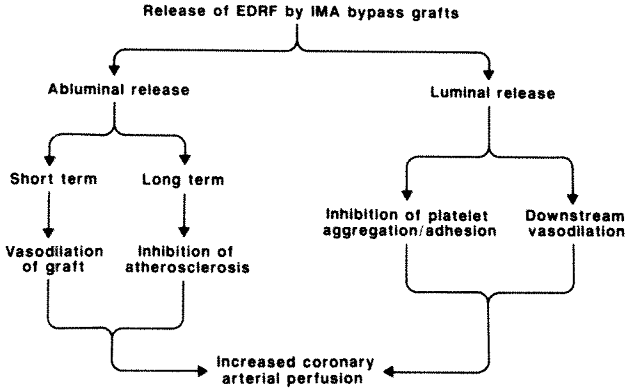

Release of EDRF by IMA bypass grafts
Abluminal release
Luminal release
Short term
Long term
Vasodilation of graft
Inhibition of atherosclerosis
Inhibition of platelet aggregation/adhesion
Downstream vasodilation
Increased coronary arterial perfusion

Fig 9. Effect of abluminal and luminal release of endothelium-derived relaxing factor (EDRF) *by internal mammary artery* (IMA) *bypass grafts.*

Supported in part by the Mayo Foundation and the CNPq Conselho de Desenvoluimento Cientifico E Technologico, Brazil.

References

1. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. N Engl J Med 1986;314:1–6.
2. Luscher TF, Diederich D, Siebenmann R, et al. Difference between endothelium-dependent relaxation in arterial and in venous coronary bypass grafts. N Engl J Med 1988;319:462–7.
3. Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide. Proc Natl Acad Sci USA 1987;84:9265–9.
4. Palmer RMJ, Ferrige AG, Moncada S. Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor. Nature 1987;327:524–6.
5. Ignarro LJ, Lippton H, Edwards JC, et al. Mechanism of vascular smooth muscle relaxation by organic nitrates, nitrites, nitroprusside and nitric oxide: evidence for the involvement of S-nitrosothiols as active intermediates. J Pharmacol Exp Ther 1981;218:739–49.
6. Ignarro LJ. Endothelium-derived nitric oxide: actions and properties. FASEB J 1989;3:31–6.
7. Radomski MW, Palmer RMJ, Moncada S. The anti-aggregating properties of vascular endothelium: interactions between prostacyclin and nitric oxide. Br J Pharmacol 1987; 92:639–46.
8. Radomski MW, Palmer RMJ, Moncada S. Endogenous nitric oxide inhibits human platelet adhesion to vascular endothelium. Lancet 1987;2:1057–8.
9. Kelm M, Schrader J. Control of coronary vascular tone by nitric oxide. Circ Res 1990;66:1561–75.
10. Pearson PJ, Lin PJ, Schaff HV. Production of endothelium-derived contracting factor is enhanced after coronary reperfusion. Ann Thorac Surg 1991;51:788–93.
11. Lin PJ, Pearson PJ, Cartier R, Schaff HV. Superoxide anion mediates the endothelium-dependent contractions to serotonin by regenerated endothelium. J Thorac Cardiovasc Surg 1991;102:378–85.
12. Rubanyi GM, Romero JC, Vanhoutte PM. Flow-induced release of endothelium-derived relaxing factor. Am J Physiol 1986;250[Heart Circ Physiol 19]:H1145–9.
13. Gillespie JS, Sheng H. Influence of haemoglobin and erythrocytes on the effects of EDRF, a smooth muscle inhibitory factor, and nitric oxide on vascular and non-vascular smooth muscle. Br J Pharmacol 1988;95:1151–6.
14. Palmer RMJ, Rees DD, Ashton DS, Moncada S. L-arginine is the physiological precursor for the formation of nitric oxide in endothelium-dependent relaxation. Biochem Biophys Res Commun 1988;153:1251–6.
15. Rees DD, Palmer RMJ, Hodson HF, Moncada S. A specific inhibitor of nitric oxide formation from L-arginine attenuates endothelium-dependent relaxation. Br J Pharmacol 1989;96: 418–24.
16. Lamontagne D, Pohl U, Busse R. N^G-nitro-L-arginine antagonizes endothelium-dependent dilator responses by inhibiting endothelium-derived relaxing factor release in the isolated rabbit heart. Pflugers Arch 1991;418:266–70.

17. Johns RA, Peach MJ, Flanagan T, Kron IL. Probing of the canine mammary artery damages endothelium and impairs vasodilation resulting from prostacyclin and endothelium-derived relaxing factor. J Thorac Cardiovasc Surg 1989;97:252–8.
18. Aarnio PT, Harjula AL, Viinikka L, Merikallio EM, Mattila SP. Prostacyclin production in free versus native IMA grafts. Ann Thorac Surg 1988;45:390–2.
19. Subramanian VA, Hernandez Y, Tack-Goldman K, Grabowski EF. Prostacyclin production by internal mammary artery as a factor in coronary bypass grafts. Surgery 1986;100:376–83.
20. Shimokawa H, Flavahan NA, Lorenz RR, Vanhoutte PM. Prostacyclin releases endothelium-derived relaxing factor and potentiates its action in coronary arteries of the pig. Br J Pharmacol 1988;95:1197–203.
21. Martin W, Villani GM, Jothianandan D, Furchgott RF. Selective blockade of endothelium-dependent and glyceryl trinitrate-induced relaxation by hemoglobin and by methylene blue in rabbit aorta. J Pharmacol Exp Ther 1985;232:708–16.
22. Garg UC, Hassid A. Nitric oxide-generating vasodilators and 8-bromo-cyclic guanosine monophosphate inhibit mitogenesis and proliferation of cultured rat vascular smooth muscle cells. J Clin Invest 1989;83:1774–7.
23. Lin PJ, Pearson PJ, Schaff HV. Endothelium-dependent contraction and relaxation of the human and canine internal mammary artery: studies on bypass graft vasospasm. Surgery 1991;110:127–35.
24. Lam JYT, Chesebro JH, Steele PM, Badimon L, Fuster V. Is vasospasm related to platelet deposition? Relationship in a porcine preparation of arterial injury in vivo. Circulation 1987;75:243–8.
25. Pohl U, Busse R. EDRF increases cyclic GMP in platelets during passage through the coronary vascular bed. Circ Res 1989;65:1798–803.
26. Moore KL. The developing human. Clinically-oriented embryology. 2nd ed. Philadelphia: Saunders, 1977:277–8.
27. Thom S, Hughes A, Martin G, Sever PS. Endothelium-dependent relaxation in isolated human arteries and veins. Clin Sci 1987;73:547–52.
28. Huddleston CB, Stoney WS, Alford WC Jr, et al. Internal mammary artery grafts: technical factors influencing patency. Ann Thorac Surg 1986;42:543–9.

DISCUSSION

DR GEORGE L. HICKS, JR (Rochester, MN): This is an elegant set of experiments, and it should be an ideal method to tell us the differences between a free graft and an in situ graft. You should be able to tell us from this set of experiments what the duration of EDRF release is and therefore the reason why free grafts may be less optimal than an in situ graft. Do you have information concerning the time frame of EDRF production?

DR PEARSON: In vivo, the limiting step of EDRF production is the availability of precursor in the blood, which is the basic amino acid L-arginine. L-arginine is taken up by the endothelial cell and is converted to nitric oxide, which is the active component of EDRF that acts as an endogenous nitrovasodilator. In the blood, the concentration of L-arginine is very high, about 10^{-6} to 10^{-5} mol/L. Thus, as long as the graft is in position with an uninterrupted supply of blood, the production of EDRF will be maintained.

DR PETER K. SMITH (Durham, NC): I was wondering if you had done the next experiment, where you would change the coronary artery used in your bioassay to perhaps explain the happy marriage between the IMA and the left anterior descending artery on a scientific basis.

DR PEARSON: We have not done those very interesting experiments that you have suggested. However, I anticipate that such experiments would demonstrate comparable results irrespective of the source of the coronary artery bioassay segment. Indeed, the superior long-term results obtained with IMA grafting of the left anterior descending coronary artery probably reflect technical considerations during grafting to the left anterior descending artery and blood flow characteristics particular to a graft supplying the left anterior descending artery in vivo. However, both surgical manipulation of a graft and blood flow through a graft can alter the release of EDRF in the bypass vessel.

DR RICHARD D. WEISEL (Toronto, Ont, Canada): Dr Pearson, I wondered whether you had looked at other grafts in addition to the IMA. Can vein grafts produce nitrous oxide or EDRF?

DR PEARSON: We have just completed studies in which we compared the luminally released vasodilator activity of effluent from perfused IMA and saphenous vein grafts. Although the effluent from the IMA and saphenous vein produce comparable vasodilation of coronary artery vascular smooth muscle, the make-up of the vasodilator activity is different between the two grafts. In the IMA, all of the vasodilator activity is due to nitric oxide, which is the active component of EDRF. In the saphenous vein graft, a large portion of the vasodilator activity is due to prostacyclin. Such a difference could account for the superior long-term patency of the IMA because not only is nitric oxide a more potent vasodilator than prostacyclin, but nitric oxide also inhibits platelet adhesion and has antiatherogenic properties on the blood vessel wall. These are two characteristics not expressed by prostacyclin.

DR ROBERT A. GUYTON (Atlanta, GA): I must ask why you chose a crystalloid solution for your perfusate. Do you not exaggerate the effects of any vascular derived vasodilators or vasoconstrictors by eliminating the metabolically active fluid that may certainly blunt any interluminal humoral effects of dilators or relaxers?

DR PEARSON: You raise a very important question: Does our model have physiological implications or can these findings only be expressed in vitro? However, experiments performed on human subjects demonstrate that if the production of endothelium-derived nitric oxide is blocked in vivo, there is a significant increase in vascular tone associated with vasoconstriction. Thus, the blockade of EDRF release in vivo with the tools we have used in the present in vitro experiments demonstrates comparable findings in peripheral arteries. I should also mention that the release of EDRF is stimulated by increasing shear stress. Thus, the responses that we measure in the bioassay system would be augmented in the high-flow state of a coronary artery bypass graft. In other words, the responses that we measure in vitro would be more pronounced in the high-flow state in vivo and could have important implications for coronary perfusion after coronary artery bypass grafting.

Coronary Artery Bypass Without Cardiopulmonary Bypass

Albert J. Pfister, MD, M. Salah Zaki, MD, Jorge M. Garcia, MD, Luis A. Mispireta, MD,
Paul J. Corso, MD, Anjum G. Qazi, MD, Steven W. Boyce, MD,
Thomas R. Coughlin, Jr, MD, and Patricia Gurny, MD

Washington Hospital Center, Washington, DC, and the Washington Adventist Hospital, Takoma Park, Maryland

The purpose of this article is twofold: to describe our technique for performing coronary artery bypass grafting without cardiopulmonary bypass (off pump) and to demonstrate that this operation is safe, in terms of mortality and certain indices of morbidity. Very little has been published in regard to off-bypass operations. From 1985 through 1990, 220 patients underwent operation off bypass; 220 on-pump controls were retrospectively matched for number of grafts, left ventricular function, and date of operation. Groups were compared in terms of mortality and ten indicators of morbidity. The same analysis was performed for ten subgroups. We found no statistically significant difference between groups in mortality (off pump, 1.4% [3/220]; on pump, 2.4% [5/220]), which held across all subgroups. Patients undergoing operation off pump required blood far less often (not transfused: off pump, 72.7% [160/220]; on pump, 54.6% [116/220]; $p = 0.005$ by Fisher's exact test), and the low output state occurred statistically less frequently off pump (off pump, 5.5% [12/220]; on-pump, 12.7% [28/220]; $p = 0.01$ by Fisher's exact test). Further research should be directed to which subgroups can be operated on to advantage off pump and which, if any, groups of patients should be confined to on-bypass operations.

(Ann Thorac Surg 1992;54:1085–92)

During the nearly three decades of coronary artery bypass grafting (CABG) experience in the United States there has been little interest in operating without cardiopulmonary bypass (CPB). Coronary artery bypass grafting with CPB has had enormous success, and the relative ease of working on the arrested heart undoubtedly makes most cardiac surgeons favor CPB in most instances. Cardiopulmonary bypass has been associated with several adverse effects. Included among these are mechanical trauma to blood components, activation of complement, impaired hemostasis, and diminished oxygen delivery. In certain cases CABG may be safer without CPB.

Coronary artery bypass grafting without CPB was successfully performed on dogs in the early 1970s [1]. Ankeney [2] reported to The Society of Thoracic Surgeons in 1972 a study of 143 patients who underwent CABG without CPB. Three years later Trapp and Bisarya [3] described their off-bypass technique used on 63 patients. In 1984, Akins and associates [4] studied the interventricular septal motion in 22 postoperative patients having had bypass grafts, 11 of whom were operated on without CPB. Although the 11 patients who underwent bypass grafting without CPB did not have the abnormal septal motion observed in the cohort having bypass grafting with CPB, it is unclear whether this observation was related to the bypass machine itself, hypothermia, or myocardial preservation techniques that were employed.

Federico Benetti [5] reported on 30 operations done off bypass between 1980 and 1983, in which the patients were selected on the basis of arterial caliber and site, without regard to clinical state or left ventricular function. It was recently reported [6] that Doctor Benetti has extended his experience in off-bypass procedures, prompted in part by limited resources and funds available in Argentina.

In this report we will describe our technique for CABG without CPB. By considering a variety of postoperative risks we will compare our results with the outcomes in a matched control group of patients operated on with CPB. We will show that this technique is safe and useful despite the theoretical loss of cardioprotection, and that certain subsets of patients may have reduced morbidity and mortality when having operation off pump.

Material and Methods

Patients

Patients whose operation was performed off bypass were selected according to certain criteria. Only those patients requiring grafts in the right coronary artery or left anterior descending coronary artery systems were eligible. Circumflex grafts are performed by torquing the heart for exposure, and our group has elected to do those on bypass. Among those eligible, our group preferentially operates on the following categories of patients off pump: (1) patients who need only grafts in the left anterior descending and right coronary artery systems; (2) patients with heavily calcified aortas, for whom the large cannulas

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Pfister, 1706 New Hampshire Ave, NW, Washington, DC 20009.

© 1992 by The Society of Thoracic Surgeons 0003-4975/92/$5.00

pose an added risk of dissection, rupture, or embolization; (3) patients who have had previous cardiac operations; (4) patients with prior cerebrovascular accidents; (5) patients on dialysis or with very impaired renal function; and (6) Jehovah's Witnesses.

Our patients were referred from urban, suburban, and rural areas in the mid-Atlantic states and were operated on in two hospitals, a 900-bed inner-city private hospital and a 300-bed suburban community hospital.

Our experimental group is composed of 220 patients who had CABG alone during the period 1985 to 1990 (with only 9 of the operations having been done before 1987) without being put on CPB. The average age of this group is 61 years, with a range of 36 to 88 years. Each patient had one or two grafts in some combination of right coronary artery, left anterior descending, and diagonal, and no patient had any other operation performed within the same anesthesia time as the CABG procedure. The total number of new grafts done in this group is 291.

Between 1985 and 1990 a total of 8,336 patients had CABG done by our group. Of these, 1,733 patients had one or two grafts performed on CPB. From this subgroup, we selected a control group of 220 patients with 291 new grafts who underwent CABG alone, on bypass, between the years 1985 and 1990. The control group was matched for year of operation, number of new grafts, and left ventricular function. In this group of patients undergoing operation on bypass, the mean pump time was 32 minutes (range, 13 to 253 minutes) and the mean aortic cross-clamp time was 17 minutes (range, 0 to 66 minutes). The average age of the control group is 59 years with a range of 32 to 86 years.

We considered ten variables affecting postoperative morbidity and mortality: hypertension, diabetes, ventricular function, renal disease, history of stroke, age, sex, reoperation, number of grafts, and graft site. We selected 11 dependent variables that we believed were related to mortality and short-term morbidity: in-hospital mortality, perioperative myocardial infarction, low output state, mechanical support, postoperative confusion, postoperative stroke, blood transfusions, superficial chest wound infections, mediastinitis, days in the intensive care unit, and days in the hospital.

Anesthetic and Surgical Technique

Anesthetic management of patients having CABG done off bypass does not differ from that employed in those patients having operation on pump. It is important to have an inotrope and an antiarrhythmic in readiness because the technique involves a certain amount of cardiac manipulation. The anesthesiologist must maintain the patient in an adequate volume status before the start of the distal anastomosis. Close monitoring of the electrocardiogram for ischemia is essential.

In the surgical procedure itself, it is helpful to tack up the cut edge of the pericardium to the chest wall to provide a firm surface on which to prop the heart as the operative field is immobilized. If it is necessary to support the heart, bolsters of laparotomy pads soaked in warm saline solution are most appropriate.

There are several guidelines specific to the main sites of distal anastomoses. Right coronary lesions are approached by providing gentle traction on the acute margin of the heart with sutures of 2-0 silk. These sutures are then held to the drapes with hemostats to provide appropriate exposure of the right coronary artery. The artery is encircled proximal and distal to the planned arteriotomy with fine silicone rubber (Quest Medical, Inc, Dallas, TX) loops or fine silk sutures, which also serve as tourniquets to interrupt blood flow. The left anterior descending coronary artery system is approached by supporting the heart on several warm, moist laparotomy pads. Proximal and distal control is usually best obtained with small, spring-loaded Bogart clamps. Alternatively, simple pressure with the blunt end of a forceps can control bleeding when the arteriotomy is made.

In general the area of the planned arteriotomy can be further immobilized with traction sutures of pledgeted suture material placed to the right and left of the planned incision. Ten thousand units of heparin is administered and allowed time to circulate before the arteriotomy is made. Gentle pressure maintained by the first assistant at sites proximal and distal to the artery aids in immobilizing it, and the anastomosis is then performed in the standard fashion. It is quite helpful to have a second assistant use a fine suction tip to keep the operative field dry. The proximal and distal clamps on the artery are released prior to snugging up the anastomosis. After completion of the procedure, the heparin is totally reversed with protamine. Should the heart demonstrate ischemic signs at any time during this procedure, the surgeon must be prepared to abandon the technique, fully anticoagulate, and place the patient on CPB.

Statistical Analysis

We used Fisher's exact test to examine the effects of the two techniques on those variables with categorical data. For ratio data we employed the nonparametric Mann-Whitney unpaired test to determine statistical significance.

Results

We eliminated renal failure and history of stroke from this analysis because there were very few cases in either group. Additionally, postoperative cerebrovascular accidents and confusion were very infrequent events, occurring equally in on-bypass and off-bypass patients. Any documented history of high blood pressure would cause a patient to be categorized as hypertensive for this study. Similarly, history of insulin use or treatment by oral hypoglycemics or diabetic diet would cause the patient to be classified as diabetic. Ventricular impairment was defined as "mild" if the ejection fraction was 0.35 to 0.45, "moderate" if 0.20 to 0.40, and "severe" if less than 0.20. The variable "redo" indicated the presence of any prior open cardiothoracic operation—nearly always previous CABG.

Patients having operation off pump are not at increased risk of mortality. Because the incidence of mortality is

Table 1. Mortality

Group	Off Pump (%)	On Pump (%)	p Value
Total (Off: 220/On: 220)	1.4	2.4	NS
Hypertension (Off: 115/On: 111)	0	2.7	NS
Diabetic (Off: 42/On: 48)	2.4	4.2	NS
Redo (Off: 47/On: 19)	2.1	10.5	NS
Elderly (Off: 24/On: 19)	4.2	10.6	NS
Female (Off: 57/On: 66)	0	1.5	NS
Normal LV (Off: 149/On: 149)	0.7	1.4	NS
Imp LV (Off: 71/On: 71)	2.8	4.2	NS
Mildly Imp LV (Off: 40/On: 40)	5.0	0	NS
Mod-Sev Imp LV (Off: 31/On: 31)	0	9.7	NS
One graft (Off: 149/On: 149)	2.0	2.0	NS
Two grafts (Off: 71/On: 71)	0	2.8	NS
Right graft (Off: 30/On: 31)	3.3	0	NS
Left graft (Off: 190/On: 189)	1.1	2.6	NS

Imp = impaired; LV = left ventricle; Mod-Sev = moderately or severely; NS = not significant.

low, it was not possible with a sample of this size to determine if, in fact, patients having operation off bypass had a statistically significant advantage in terms of mortality, as a visual inspection of the data might suggest (Table 1).

The data in Table 2 convincingly demonstrate that patients operated on without CPB are more likely to avoid blood transfusions entirely. Only a few subgroups failed to attain statistically significant differences between on-pump and off-pump groups, but all of those groups did exhibit a numerical advantage for off-pump cases in this study.

Postoperative low output syndrome was defined as the condition in which inotropic drug support was required for more than 24 hours for the purpose of generating an adequate cardiac output. The incidence of low output and intraaortic balloon pump use is higher (except for redo operations) for patients having operation on bypass. This difference reached statistical significance for the total group and many categories therein (Table 3).

Table 2. Percentage of Patients Not Transfused[a]

Group	Off Pump (%)	On Pump (%)	p Value
Total	72.7	54.6	<0.005
Hypertension	74.8	52.2	<0.005
Diabetic	69.0	39.6	0.006
Redo	70.2	47.4	0.09
Elderly	54.2	36.8	NS
Female	63.2	43.9	0.04
Normal LV	75.4	58.4	0.002
Imp LV	66.2	46.5	0.03
Mildly Imp LV	67.5	50.0	NS
Mod-Sev Imp IV	64.6	41.9	0.12
One graft	72.5	61.0	0.05
Two grafts	73.2	40.8	<0.005
Right graft	60.0	48.4	NS
Left graft	74.4	55.5	<0.005

[a] Abbreviations and numbers of patients in each group are the same as in Table 1.

Table 4 shows incidence of perioperative myocardial infarction (MI). Determining whether or not a perioperative MI has occurred is a special problem recognized as such in the literature. The usual diagnostic criteria may fail to secure a diagnosis. In our patient population, we defined a perioperative MI as: (1) the development and persistence of new Q-waves on the electrocardiogram, (2) poor R-wave progression in the precordial leads that was not present preoperatively, or (3) an absolute creatine kinase-MB band greater than 50 ng/mL.

Because of the discrepancy in size between experimental and control groups for redo operations (19 operations done on pump versus 47 redo operations done off bypass), we took the analysis of the redo data a step further. We attempted to make another matched group for redo operations, controlled for left ventricular function and date of operation, selecting patients from a population of all patients having redo operation with one or two new grafts regardless of graft site done on pump during the period of this study, which numbered 181. We failed to locate an equal number of matched cases; however, we did compare 44 matches we found with the 47 done off pump. The results are tabulated in Table 5.

We defined mediastinitis as a deep infection requiring return to operating room for debridement and closure by any method deemed appropriate. Superficial infections were defined as infection confined to tissues external to the sternum, which can be treated at the bedside (Table 6).

The last two dependent variables that we examined were measured as ratios (Table 7). Because days in the intensive care unit and in the hospital cannot be less than zero, and can extend far beyond the mean in upper limit, we used the nonparametric Mann-Whitney unpaired test to determine statistical significance. Days in the hospital may be misleading, although the error is systematic and should affect all categories equally, because it may include preoperative days for those patients who underwent catheterization and were then operated on during the same admission.

Comment

The major conclusion that we have made based on our data is that select patients can safely undergo CABG without CPB support. The most attractive aspect of off-bypass operations is the marked decrease in the need for postoperative transfusions. Had we included the intraoperative data, the advantage would have been more marked: 70% not transfused in the off-bypass patients and 45% not transfused among the on-pump patients. This advantage held up across all subgroups examined. A few groups—elderly patients, those with mildly impaired ventricles, and those with right grafts—had differences favoring the off-bypass group that did not achieve statistical significance. In the case of elderly patients, we might

Table 3. Percentage of Patients Having Low Output Syndrome or Requiring Intraaortic Balloon Pumping[a]

	Low Output			Intraaortic Balloon Pump		
Group	Off Pump (%)	On Pump (%)	*p* Value	Off Pump (%)	On Pump (%)	*p* Value
Total	5.5	12.7	0.01	0.9	3.6	0.11
Hypertension	5.2	18.0	0.003	0.9	4.6	0.11
Diabetic	4.8	16.7	0.09	2.4	0	NS
Redo	10.6	10.5	NS	2.1	0	NS
Elderly	16.7	31.6	NS	16.7	31.6	NS
Female	8.8	22.7	0.04	0	4.5	NS
Normal LV	4.7	6.7	NS	0.7	0	NS
Imp LV	7.0	25.4	0.005	1.4	11.3	0.03
Mildly Imp LV	7.5	17.5	NS	2.5	7.5	NS
Mod-Sev Imp LV	6.5	35.5	0.01	0	16.1	0.05
One graft	5.4	12.1	0.06	1.3	3.9	NS
Two grafts	5.6	14.1	0.15	0	4.2	NS
Right graft	13.3	16.1	NS	0	3.3	NS
Left graft	4.2	12.2	<0.005	1.1	3.7	0.10

[a] Abbreviations and numbers of patients in each group are the same as in Table 1.

hypothesize that the physicians may be more liberal with their use of blood products as resuscitative fluids.

The second major advantage accrued to those patients undergoing operation off pump is a decrease in the low cardiac output syndrome. Except for our initial comparison of patients having redo operations, all other groups, including those having redo operations when compared with all those having redo operations done on pump and with the group of incompletely matched patients having redo operations, had fewer occurrences of the low output state postoperatively. This correlation was particularly strong for moderate to severely impaired ventricles. The research of Akins and associates [4] regarding detrimental effects on the ventricular septum may offer some explanation of this finding. It may be true that new septal dysfunction in previously impaired hearts is poorly tolerated, leading to the low output state. As shown in Table 3, the need for intraaortic balloon pump support reflected the incidence of low output state postoperatively, but with fewer cases; this, of course, obviated a statistical argument.

We were surprised to find that the incidence of perioperative MI did not "predict" mortality; that is, in many of the subgroups—diabetics, elderly, redo operations, normal left ventricles, mildly impaired left ventricles, and two-graft operations—mortality varied inversely with MI. There are several possible explanations for this. Diagnosis of perioperative MI is often difficult and not clear-cut. On the other hand, the low incidence overall of both mortality and perioperative MI with the resulting failure to achieve statistical significance may actually indicate that the differences we see are truly those of "chance," and in a larger series the occurrence of MI might well predict mortality. It is not unreasonable to suppose that lack of cardioprotection as occurs with off-bypass cases may predispose to perioperative infarct, and it would be useful

Table 4. Percentage of Patients Having Perioperative Myocardial Infarction[a]

Group	Off Pump (%)	On Pump (%)	*p* Value
Total	5.5	7.7	NS
Hypertension	6.1	8.1	NS
Diabetic	7.1	4.2	NS
Redo	12.8	0	NS
Elderly	12.5	10.5	NS
Female	7.0	7.6	NS
Normal LV	3.4	2.0	NS
Imp LV	9.9	19.7	0.15
Mildly Imp LV	7.5	22.5	0.11
Mod-Sev Imp LV	12.9	16.1	NS
One graft	5.4	9.4	NS
Two grafts	5.6	4.2	NS
Right graft	6.7	16.0	NS
Left graft	5.3	6.3	NS

[a] Abbreviations and numbers of patients in each group are the same as in Table 1.

Table 5. Comparison of All Redo Operations, Redo Operations Done Off Pump, and a Matched Redo On-Pump Group

	All Redos		Off Pump		Matched
Variable	%	*p* Value	%	*p* Value	Redo (%)
Mortality	10.0	NS	2.3	NS	6.6
MI	11.2	NS	12.8	NS	11.4
Low output	19.9	NS	9.1	0.034	26.7
No transfusion	48.6	0.006	70.4	0.057	

MI = myocardial infarction; NS = not significant.

Table 6. Percentage of Patients With Mediastinitis and Superficial Infection[a,b]

	Mediastinitis			Superficial Infection		
Group	Off Pump (%)	On Pump (%)	*p* Value	Off Pump (%)	On Pump (%)	*p* Value
Total	1.0 (2)	1.8 (4)	NS	2.7 (6)	0.5 (1)	NS
Redo	0	0	NS	4.3 (2)	0	NS
Hypertension	1.8 (2)	1.8 (2)	NS	4.3 (5)	0.9 (1)	NS
Female	1.8 (1)	0	NS	3.5 (2)	0	NS
Elderly	0	0	NS	0	0	NS
Diabetic	4.8	2.1 (1)	NS	7.1 (3)	0	0.10
CVA	0	0	NS	11.1 (1)	0	NS
Renal	0	0	NS	0	0	NS
Normal LV	0.7 (1)	2.0 (3)	NS	1.3 (2)	0	NS
Imp LV	1.4 (1)	1.4 (1)	NS	5.6 (4)	1.4	NS
Mildly Imp LV	2.5 (1)	0	NS	2.5 (1)	0	NS
Mod-Sev Imp LV	0	3.2 (1)	NS	9.7 (3)	3.2 (1)	NS
One graft	1.4 (2)	2.0 (3)	NS	3.4 (5)	0	0.06
Two grafts	0	1.4 (1)	NS	1.4 (1)	1.4 (1)	NS
Right graft	0	6.5 (2)	NS	6.5 (2)	0	NS
Left graft			NS			NS

[a] Numbers of patients in each group are the same as in Table 1. [b] Numbers in parentheses are numbers of patients in each category.

CVA = cerebrovascular accident; all other abbreviations are the same as in Table 1.

to pursue follow-up studies on left ventricular function by echocardiography or multigated acquisition scans after off-bypass operations to establish risk to the myocardium from this procedure, as none of our variables dealt with long-term outcomes and no adverse effects were apparent in the short-run.

The data on the infection rates indicate no differences between the groups in regard to mediastinitis; however, diabetics undergoing operation on bypass have fewer infections, although this is not statistically significant. The increased incidence of superficial infections found in off-pump patients is puzzling. Because length of hospitalization does not seem to be affected, the importance of this observation may be minimal, although future research should track this finding.

Although there were essentially no statistically significant differences between the two groups in regard to length of hospitalization, it is obvious from Table 7 that

Table 7. Intensive Care Unit and Hospital Stay[a,b]

	ICU Stay (days)			Hospital Stay (days)		
Group	Off Pump	On Pump	*p* Value	Off Pump	On Pump	*p* Value
Total	1.82 ± 2.64	2.64 ± 7.14	NS	10.45 ± 5.45	12.27 ± 13.25	NS
Hypertension	1.81 ± 2.55	2.62 ± 4.41	NS	10.95 ± 6.06	12.73 ± 12.11	NS
Diabetic	2.00 ± 3.03	2.26 ± 3.83	NS	11.75 ± 6.55	13.42 ± 14.06	NS
Elderly	3.04 ± 4.86	4.05 ± 5.66	NS	13.30 ± 6.96	18.44 ± 20.73	NS
Female	1.59 ± 1.27	2.87 ± 4.39	NS	10.79 ± 3.74	13.82 ± 13.41	NS
Redo	2.79 ± 4.64	2.47 ± 3.31	NS	12.36 ± 6.20	11.67 ± 5.50	NS
All redos		4.56 ± 12.31			13.27 ± 15.72	
Including match		2.68 ± 3.32			11.43 ± 5.48	
Normal LV	1.68 ± 2.33	2.41 ± 8.23	NS	10.13 ± 5.61	12.05 ± 14.73	NS
Impaired LV	2.16 ± 3.23	3.13 ± 3.91	0.04	11.14 ± 5.06	12.90 ± 9.34	NS
Mild	2.08 ± 3.21	3.06 ± 3.84	NS	11.13 ± 4.89	10.75 ± 5.23	NS
Mod-Sev	2.21 ± 3.08	3.21 ± 4.07	NS	11.85 ± 6.31	15.78 ± 12.50	NS
One graft	1.65 ± 2.18	2.41 ± 8.00	NS	10.35 ± 5.10	11.41 ± 12.56	NS
Two grafts	2.22 ± 3.36	3.09 ± 5.19	NS	10.64 ± 6.10	14.10 ± 14.47	NS
Right graft	1.54 ± 1.18	2.10 ± 2.74	NS	11.25 ± 4.07	13.17 ± 7.73	NS
Left graft	1.86 ± 2.78	2.73 ± 7.64	NS	10.34 ± 5.61	12.12 ± 13.97	NS

[a] Values are shown as mean ± standard deviation. [b] Numbers of patients in each group are the same as in Table 1.

ICU = intensive care unit; all other abbreviations are the same as in Table 1.

the experimental group spent less time in the intensive care unit and in the hospital. The interesting point to be made is that the patients who did not undergo CPB had a far more homogeneous postoperative course as indicated by the much smaller standard deviations recorded (except for redo operations). This is another area worthy of further investigation, to decide whether this phenomenon was part of the vagaries of our sample selection or if a bypass procedure in specific patients begets further complications for them, and if so, whether we can identify those patients preoperatively.

Our intervening variables (subgroups) could be divided into three categories: demographic variables, disease variables, and technical variables. The demographic variables (age and sex) demonstrated successful outcomes in the operations done off pump. In the literature, female patients have frequently suffered greater mortality and morbidity than male patients. In our sample, female patients have low mortality rates relative to other subgroups and to the total group, whether done on or off bypass, but had higher rates of morbid events such as low output, higher transfusion rates, and more MIs than many other categories of patients. Female patients did better when their operations were done off pump, across all parameters, leaving us to speculate about why women cannot expect the same success rate from CPB as men.

We were very interested in the outcomes for the group of patients aged 75 years and older, because we usually attempted to operate on patients with acceptable anatomy who demonstrated extensive aortic calcification off pump, a situation expected to occur more frequently in the elderly population. Unfortunately, owing to small sample size (24 off pump and 19 on pump), statistical significance could not be achieved. However, across all categories, elderly patients did better postoperatively if they were operated on without CPB. Of particular note, the length of hospital stay was much longer for the on-pump patients and had larger variation than demonstrated by the other variables, suggesting that some elderly patients have excessive numbers of complications lengthening their hospitalizations if they are operated on with CPB. In addition, although not presented in the data analysis section because postoperative confusion occurred infrequently in other groups of patients, on-pump elderly patients experienced more than three times the incidence of postoperative confusion than did those undergoing operation off pump (15.8% versus 4.2%).

In the analysis of disease state variables, diabetics and hypertensives each derived benefit from being operated on without CPB, significantly so in terms of low output and transfusions. Mediastinitis developed more than twice as frequently in diabetics, in whom infection is a problem, if their operation was done off pump, although overall length of hospital stay was still lower for off-pump patients. The explanation for this is not obvious, but it should alert other groups that risk of infection in diabetics may be increased off bypass.

The data on left ventricular function resembled those in all other groups. It should be noted that the group of patients with mildly impaired ventricles, even though deriving benefit from off-bypass operation in regard to postoperative low output, had a smaller percentage of untransfused patients than did other groups, and a higher (not significant) mortality than those with mildly impaired ventricles having operation on bypass. The patients with more severely impaired left ventricles derived far greater advantage from off-pump technique across all dependent variables as noted earlier than did any other category of patient except the elderly. Research focused on marginal ventricles and elderly patients may well be able to establish clear-cut and significant benefit for these groups in mortality and length of hospitalization.

We were forced to eliminate the groups of patients with prior cerebrovascular accidents and those with severe renal disease from our analysis because of inadequate sample size. We believe that future research on off-pump operations should look specifically at these two groups, in that those patients with a bleeding diathesis such as severe renal impairment and whose cerebral function may not tolerate inadequate cardiac output might be spared the increased risk of mortality that these groups undergo for CABG.

Our group was particularly interested in one of the technical variables—redo operations—because that is another category that we generally attempt to operate on without CPB. As underscored previously this selectivity produced a very unequal distribution of redo operations between the on-pump and off-pump groups. Most importantly, even failing to achieve statistical significance, the incidence of mortality in the on-pump group was five times that of the off-pump group in two of the three redo comparisons and three times greater in the incompletely matched group with redo operations. The patients having off-bypass redo operations also maintained an advantage in terms of fewer patients transfused, and two of the three redo on-pump groups had greater incidence of low output. Because of the seeming advantage in mortality, comparison of groups of equal size, with similar controls, may confirm that off-bypass operation is the procedure of choice for redo operations not requiring circumflex grafts. There was little difference between the one- and two-graft operations done off pump for most dependent variables (patients with two grafts spent a day longer on average in the intensive care unit, although total hospitalizations were essentially the same). Patients having two-graft operations done on pump did slightly less well than their one-graft counterparts. From our data, the results for both one and two grafts show the same advantage as the off-pump group as a whole; it does not appear that needing either one or two grafts should influence the decision to operate with or without CPB.

The anatomy variable—right graft only versus any left graft—displayed some curious results. It may be a function of small sample size (30) that the group with right graft only did not demonstrate the same advantages for off-bypass patients, whereas the group with any left graft did as well as the group in general against on-pump patients. It may also be that the patients with right grafts only had right-dominant anatomy with major areas of myocardium either previously injured or at great risk, or that other medical conditions or general state of health persuaded the clinicians to operate for a right-sided lesion, thereby increasing the risk profile in this group relative to the left-graft patients.

A further concern, the issue of complete revascularization in off-pump operations, was mentioned in an article that appeared after the present research was completed [7]. Although it is true that invasive cardiologists have usurped many of the straightforward one- and two-graft cases with apparent success, there are still many patients with that anatomy who come to the operating room in our practice: patients with failed angioplasties, those with multiple prior angioplasties and recurrent stenoses, patients having long, irregular lesions, and patients who simply opt for operation. The very fact that angioplasty itself has gained acceptance in the medical community is an argument in support of off-bypass procedures, given that percutaneous transluminal coronary angioplasty is an off-pump technique offering less protection to the patient than off-pump operation. In our practice, only those patients who would be "completely revascularized" by the proposed operation underwent the procedure off bypass.

Furthermore, we have taken the stand that CABG could be performed without CPB only if there is an indication to do so. These have been listed previously. We do not believe it is a procedure to be done simply because it can be done.

In summary, it seems evident from our data that off-bypass procedures in select patients are safe and in some ways advantageous for patients. The data also seem to suggest that certain groups of patients—those with more impaired left ventricles, women, hypertensives, and especially the elderly and those patients needing a redo operation—may garner marked advantage from this technique and should therefore be the subject of future research. Although in general, diabetics do well if operated on without bypass, the issue of risk from infection needs to be further delineated before any recommendations for diabetics can be made.

References

1. Kluge TH, Kerth WJ, Gerbode F. Aorto-coronary bypass in experimental animals without the use of extracorporeal circulation. Scand J Thorac Cardiovasc Surg 1972;6:257–61.
2. Ankeney JL. Coronary vein graft without cardiopulmonary bypass. Surgical motion picture presented at annual meeting of The Society of Thoracic Surgeons, Jan 1972.
3. Trapp WG, Bisarya R. Placement of coronary artery bypass graft without pump oxygenator. Ann Thorac Surg 1975;19:1–9.
4. Akins CW, Boucher CA, Pohost GM. Preservation of interventricular septal function in patients having coronary artery bypass grafts without cardiopulmonary bypass. Am Heart J 1984;107:304–9.
5. Benetti FJ. Direct coronary surgery with saphenous vein bypass without either cardiopulmonary bypass or cardiac arrest. Cardiovasc Surg 1985;26:217–22.
6. The Loma Linda Report: LLUMC surgeons perfect new technique. Advent Rev 1990.
7. Buffolo E, Andrade JCS, Branco JNR, Aguiar LF, Ribeiro EE, Jatene AD. Myocardial revascularization without extracorporeal circulation: seven year experience in 593 cases. Eur J Cardiothorac Surg 1990;4:504–8.

DISCUSSION

DR CARY W. AKINS (Boston, MA): I congratulate Dr Pfister on his interesting presentation of a provocative subject. Cardiopulmonary bypass allows surgeons to address lesions that were inaccessible or carry an exorbitant risk. However, this advancement has a price, which cardiac surgeons have recently begun to truly understand. Thus there is some innate attractiveness to performing myocardial revascularization while avoiding potential deleterious effects of cardiopulmonary bypass.

Unfortunately, performing coronary artery grafting without bypass has occasionally been called a triumph of technique over reason. Although the technique is excellent for some patients, I am certain its widespread, indiscriminate use is wrong. I agree with Pfister and associates that the indications for this procedure should be patient-related, not surgeon-related.

My experience with coronary artery grafting without bypass includes 47 patients with no mortality. Our selection criteria focused on the coronary anatomy, specifically patients with totally occluded or tightly stenotic, well collateralized and easily accessible left anterior descending or right coronary artery lesions.

Today's presentation documents the low risk of coronary artery grafting without bypass in 220 patients. Then Pfister and associates retrospectively compared the off-bypass group with an on-bypass group, matched only for number of vessels grafted, operative year, and left ventricular function. They inferred certain advantages to the off-bypass technique, related to blood conservation and other aspects of morbidity and mortality. Unfortunately the groups were importantly different in other characteristics and not comparable.

The statistical methods used to assess these cohorts are inappropriate to address the questions asked. Univariate analysis of treatment outcomes in disparate cohorts is not appropriate; rather they should use multivariate regression analysis with procedure performed as a variable. Additionally necessary but unstated variables are incidence of recent infarction, operative priority, preoperative red cell mass, and use of arterial conduits. Also, the study reports only in-hospital events; as important are long-term results, particularly graft patency.

What coronary anatomic features do you use to select patients? Has eschewing bypass caused you to avoid using arterial grafts to the anterior descending system in any patient? In how many patients did ischemia develop requiring use of cardiopulmonary bypass? What is your graft patency?

DR PFISTER: All of the members of our group share Dr Akins' concern with regard to the safety of the technique and the indications that are used to apply it to patients. I have tried to stress that our decision to use the technique depends on identifying a patient population for whom we believe it may be beneficial. We do not compromise the patient on either bypass conduit, number of grafts, or completeness of revascularization in an attempt to use this over standard cardiopulmonary bypass techniques. As pointed out in the presentation, a very high percentage of patients receive mammary artery grafts.

There have been fewer than 10 cases in which we had to go on bypass because of ischemia. We set up the anastomosis and then wait for a brief period of time before performing the arteriotomy. This allows us to see how the patient tolerates the manipulation and vessel occlusion necessary for the technique. There have been episodes in which we have misread the artery and have gone on bypass and completed the anastomosis because we believed that technically an accurate job could not be done off bypass.

Dr Akins' statistical concerns may be valid. We continue to use the procedure in selected patients and will continue to analyze our data.

DR STEVEN R. GUNDRY (Loma Linda, CA): Beginning in 1989 after the return of one of my colleagues from a fellowship in South America to learn these techniques, our group as a whole decided to attempt off-bypass revascularization in all patients undergoing coronary revascularization, and in fact in 1989 was able to accomplish this in 128 patients. We applied a mean number of three grafts per patient with a range of from one to five grafts. Anatomy was not considered a detriment to the performing of these arterial grafts, and in fact direct attack on the circumflex and posterolateral systems was done using very novel techniques developed in South America.

In perhaps our enthusiasm and excitement for this technique two of my colleagues reported our results last year, and indeed found very similar results to what Pfister and associates have found today, such as slightly less hospital stay, less blood loss, and a very good in-hospital mortality.

Unfortunately, in the year after that experience, we have found in this patient cohort a number of quite early and late deaths, and an unfortunately large number of patients have returned to our institution with recent onset angina. Those patients who have had angiograms have had an inordinate number of graft stenoses at anastomotic sites and have had an inordinate number of stenoses at the sites of the stay sutures or loops placed around vessels to give a good operative field. Because of this finding we have totally abandoned this technique at Loma Linda University and I do not recommend it to our members.

I do have one question. What is your follow-up in terms of angiography of the patients who have been studied, and have there been any early or late deaths out of the hospital that you have had autopsy results for?

DR PFISTER: Long-term follow-up was not addressed in this study because the care for our patients reverts back to the referring cardiologist at 2 months postoperatively. Although we have not insisted on routine recatheterizations in these patients, they do undergo exercise stress testing 6 weeks after operation and then yearly. Because our referral base is very loyal to the institution, if there were recurrent problems with these patients, I feel very confident that we would have been made aware. Many of these patients have been followed up for 3 or more years after operation. Of these 220 people, I am aware of only 1 patient who returned with recurrent symptoms. Recatheterizations showed an anastomotic narrowing that was treated quite successfully with balloon dilation.

With proper patient selection, our experience clearly demonstrates that coronary artery bypass grafting without cardiopulmonary bypass can be done in a safe and beneficial manner.

Left Atrial Isolation Associated With Mitral Valve Operations

Angelo Graffigna, MD, Francesco Pagani, MD, Gaetano Minzioni, MD,
Jorge Salerno, MD, and Mario Viganò, MD

Cattedra di Cardiochirurgia and Cattedra di Cardiologia, Università degli Studi di Pavia and IRCCS Policlinico S. Matteo, Pavia, Italy

Surgical isolation of the left atrium was performed for the treatment of chronic atrial fibrillation secondary to valvular disease in 100 patients who underwent mitral valve operations. From May 1989 to September 1991, 62 patients underwent mitral valve operations (group I); 19, mitral valve operations and DeVega tricuspid annuloplasty (group II); 15, mitral and aortic operations (group III); and 4, mitral and aortic operations and DeVega tricuspid annuloplasty (group IV). Left atrial isolation was performed, prolonging the usual left paraseptal atriotomy toward the left fibrous trigone anteriorly and the posteromedial commissure posteriorly. The incision was conducted a few millimeters apart from the mitral valve annulus, and cryolesions were placed at the edges to ensure complete electrophysiological isolation of the left atrium. Operative mortality accounted for 3 patients (3%). In 79 patients (81.4%) sinus rhythm recovered and persisted until discharge from the hospital. No differences were found between the groups (group I, 80.7%; group II, 68.5%; group III, 86.7%; group IV, 75%; p = not significant). Three late deaths (3.1%) were registered. Long-term results show persistence of sinus rhythm in 71% of group I, 61.2% of group II, 85.8% of group III, and 100% of group IV. The unique risk factor for late recurrence of atrial fibrillation was found to be preoperative atrial fibrillation longer than 6 months. Due to the satisfactory success rate in recovering sinus rhythm, we suggest performing left atrial isolation in patients with chronic atrial fibrillation undergoing valvular operations.

(Ann Thorac Surg 1992;54:1093–8)

Atrial fibrillation is present in 40% to 50% of patients with rheumatic valve disease; the risk is greater for patients with mitral valve disease than for those with aortic valve disease, and for those with mitral valve incompetence than for those with mitral valve stenosis. Prevalence increases with patients' age and functional class, with the duration of the disease, and with left atrial size [1–6].

Pathogenesis of atrial fibrillation in such patients is still debated: most authors agree that rheumatic inflammation and hemodynamic burden cause an increase in tissue fibrosis and an inhomogeneous distribution of diastolic depolarization potentials, refractory periods, and conduction properties within the atrial muscle [4, 7–11]. All these factors enhance the probabilities of reentry circuits around areas with longer refractory periods. Such circuits take place in ever-changing areas of pathologic tissue, while other atrial areas are passively activated. A critical atrial surface area appears to be necessary for atrial fibrillation to endure, which explains the greater incidence of atrial fibrillation in patients with larger atrial chambers.

Several authors admit that after operation atrial fibrillation recurs in 35% to 80% of patients with long-standing atrial fibrillation [12–18]. Nevertheless, restoration of sinus rhythm could allow an optimal cardiac output and could avoid the necessity of therapy for the control of fast atrial fibrillation.

With the premise that the presence of an enlarged and diseased left atrium could maintain atrial fibrillation postoperatively, we decided to associate the electrophysiologic isolation of the left atrium [19] to mitral valve procedures in patients with chronic (longer than 3 months) atrial fibrillation. The aim of the procedure was to prevent the spread of the arrhythmia from the enlarged left atrium to the atrial septum and to the right atrium so that sinus activation of the right atrium could be conducted to the ventricles.

Material and Methods

Surgical Technique

The patients are customarily studied by means of bidimensional and Doppler ultrasonography, as well as coronary artery angiography if suggested by age or symptoms. All of them gave informed consent to the procedure.

After median sternotomy cardiopulmonary bypass with double- or single-stage atrial cannulas is commenced. Myocardial protection is achieved by means of antegrade St. Thomas' cardioplegia injection and topical pericardial cooling.

A left paraseptal atriotomy is performed: the caudal edge of the incision is prolonged toward the posterome-

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Graffigna, Cattedra di Cardiochirurgia, IRCCS Policlinico S. Matteo, P.le Golgi 4, 27100, Pavia, Italy.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

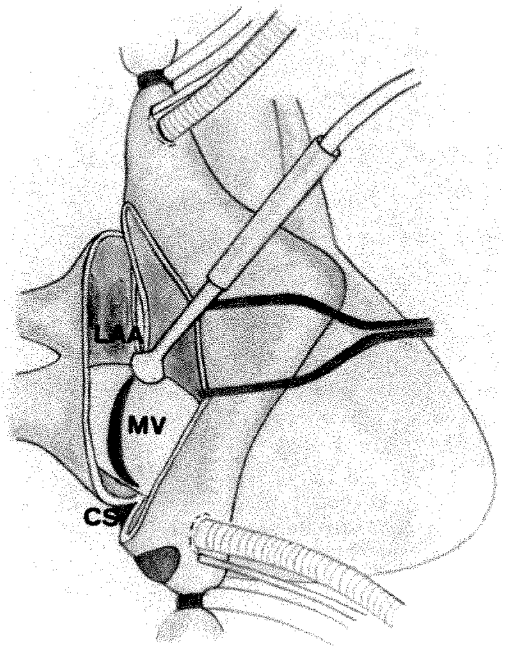


Fig 1. Surgical technique of left atrial isolation. (CS = *coronary sinus;* LAA = *left atrial appendage;* MV = *mitral valve.)*

dial commissure of the mitral valve as far as a few millimeters from the mitral valve annulus, taking care not to sever the terminal portion of the coronary sinus, which often courses within the atrial wall, and any right or left coronary artery branches. The cranial edge of the atriotomy is conducted along the atrial roof and toward the left fibrous trigone, just anteriorly to the left atrial appendage opening, ending a few millimeters from the mitral valve annulus; in this position it is important to safeguard the proximal circumflex artery.

At the edges of the incisions two overlapping cryolesions are placed at −60°C for 120 seconds to sever atrial fibers closer to the mitral valve annulus (Fig 1). It is advisable to place an additional cryolesion on the external wall of the coronary sinus owing to the presence of conducting fibers between right and left atria.

At this point the mitral valve is repaired or excised and replaced, and left atrium is reconstructed. Tricuspid valve annuloplasty or aortic valve replacement are performed last.

Table 1. Mitral Valve Pathology of Patients Who Underwent Left Atrial Isolation

Group[a]	S	I	SI	Re-st	Deg	PVE	Total
I	20	12	21	7	1	1	62
II	6	3	6	4	. . .	. . .	19
III	5	. . .	8	1	1	. . .	15
IV	1	. . .	3	. . .	. . .	. . .	4
Total	32	15	38	12	2	1	100

[a] For the operative groups, see Figure 3.

Deg = degeneration of bioprosthetic valve; I = incompetence; PVE = prosthetic valve endocarditis; Re-st = stenosis after closed heart commissurotomy; S = stenosis; SI = stenosis and incompetence.

Table 2. Surgical Procedures on the Mitral Valve

	Replacement				
Group[a]	Total	S	I	Repair	Commissurotomy
I	48	46	2	11	3
II	17	17	. . .	2	. . .
III	15	15	. . .	. . .	. . .
IV	2	2	. . .	1	1
Total	82	80	2	14	4

[a] For the operative groups, see Figure 3.

I = interrupted sutures; S = single 2-0 Prolene running suture.

A supplement of approximately 17 minutes of cross-clamping time is required to perform the procedure, which can be further shortened by using a double cryoprobe freezing system.

Three pairs of electrodes are placed on the left and right atrial appendages and on the right ventricle for sensing and pacing purposes. Left atrial isolation is tested by means of unipolar electrograms from right and left atrial electrodes, and by evaluating if left atrial stimulation is not conducted to the right atrium; this procedure is performed daily to evaluate left atrial activity.

All patients were studied at 1 month from operation, and then yearly with surface electrocardiography and clinical evaluation.

Table 3. Risk Factors for Lack of Recovery of Sinus Rhythm

		AF		
Factor	Total	No.	%	p Value
Sex				NS
M	22	7	31.8	
F	78	14	17.9	
Age				NS
<50 years	35	5	14.2	
>50 years	65	16	24.6	
Preoperative AF duration				<0.05
<6 mo	18	0	0	
>6 mo	82	18	21.9	
Mitral valve pathology				NS
Stenosis	32	8	25	
Stenosis/incompetence	38	7	18.4	
Incompetence	15	4	26.6	
Restenosis	12	1	8.3	
BVD	2	. . .	0	
PVE	1	. . .	0	
Operative group				NS
I	62	12	19.3	
II	19	6	31.5	
III	15	2	13.3	
IV	4	1	25	

AF = atrial fibrillation; BVD = bioprosthetic valve degeneration; F = female; M = male; NS = not significant; PVE = prosthetic valve endocarditis.

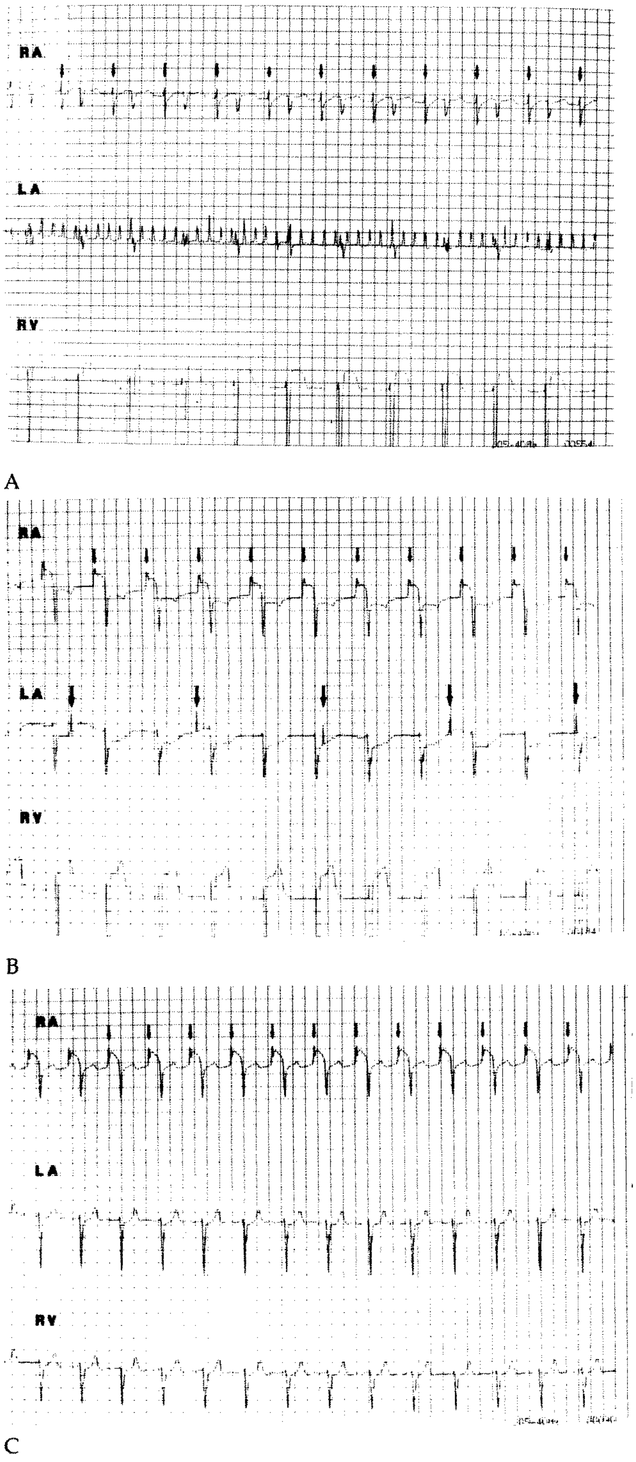


Fig 2. Postoperative behavior of the isolated left atrium during sinus rhythm: fibrillation (A), intrinsic rhythm at low rate (B), and absence of electrical activity (C). Traces are unipolar registrations from right atrial (RA), *left atrial* (LA), *and right ventricular* (RV) *epicardial electrodes.*

Table 4. Risk Factors for Recurrence of Atrial Fibrillation

Factor	Total	AF No.	AF %	*p* Value
Sex				NS
M	21	9	42.8	
F	76	18	23.6	
Age				NS
<50 years	35	8	22.8	
>50 years	62	19	30.6	
Preoperative AF duration				<0.05
<6 mo	18	0	0	
>6 mo	79	23	29.1	
Mitral valve pathology				NS
Stenosis	31	9	29	
Stenosis/incompetence	36	8	22.2	
Incompetence	15	7	46.6	
Restenosis	12	2	16.6	
BVD	2	. . .	0	
PVE	1	1	100	
Operative group				NS
I	62	18	29	
II	18	7	38.8	
III	14	2	14.2	
IV	3	0	0	

For abbreviations, see Table 3.

Patient Population

From May 1989 to September 1991, 100 patients underwent the left atrial isolation procedure in association with a mitral valve operation. Patients had isolated mitral valve disease (62 patients, group I), mitral and tricuspid valve disease (19 patients, group II), mitral and aortic valve disease (15 patients, group III), or combined mitral, aortic, and tricuspid valve disease (4 patients, group IV). Mitral valve pathology is reported in Table 1.

Twenty-eight patients had suffered from arterial limb (11 patients) or central nervous system (17 patients) embolism. Atrial fibrillation was present for more than 6 months in 94 patients, and for less than 6 months but longer than 3 months in 18.

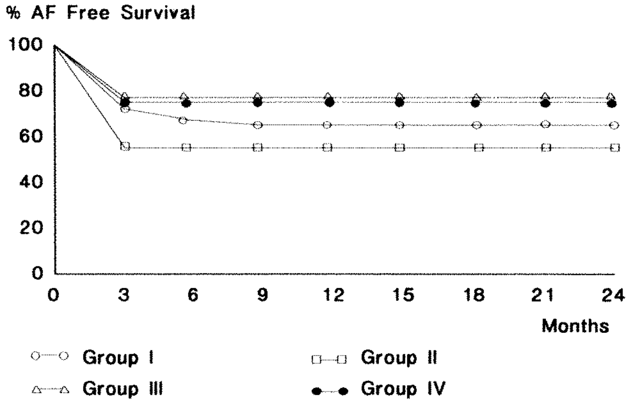


Fig 3. Actuarial survival rates and freedom from atrial fibrillation (AF). (Group I = *mitral valve procedure;* Group II = *mitral and tricuspid valve procedures;* Group III = *mitral and aortic valve procedures;* Group IV = *mitral, aortic, and tricuspid valve procedures.)*

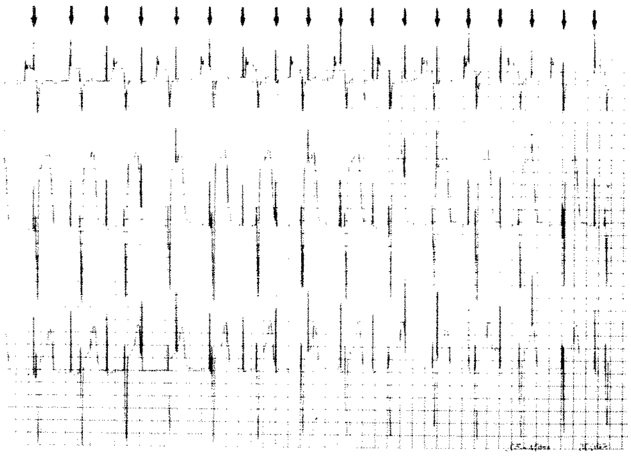


Fig 4. Test for the effectiveness of left atrial isolation. Left atrial pacing (arrows) does not capture right atrium and ventricles. Traces are unipolar registrations from right atrial (RA), left atrial (LA) and right ventricular (RV) epicardial electrodes.

The mitral valve was replaced in 82 patients and repaired in 18 (4 open heart commissurotomies; Table 2). Associated procedures were the exclusion of the left atrial appendage (7 patients), coronary artery bypass grafting (2 patients), and aortic subvalvular myectomy and epicardial interruption of a Kent bundle (1 patient each).

Results

Three cases of operative (less than 30 days) mortality are reported, due to cardiorespiratory failure (2 patients on days 5 and 32) and multiple organ failure (1 patient on day 40).

Among the operative complications there were 8 cases of low output syndrome (2 requiring intraaortic balloon pump), 5 cases of respiratory insufficiency, 4 cases of major ventricular arrhythmias, and 2 cases of sternal wound infections. There were 2 cases of temporary atrioventricular block and 3 cases of permanent atrioventricular block that required implantation of a permanent ventricular pacemaker.

Left atrial isolation was effectively performed in 88 patients (88%), as detected by left atrial stimulation. Sinus rhythm was restored in 79 patients (81.4%) and was maintained until discharge from the hospital. There was no significant difference in restoration of sinus rhythm among the groups: 80.7% in group I, 68.5% in group II, 86.7% in group III, and 75% in group IV (Table 3). The mean P-R interval in patients who gained sinus rhythm was 220 milliseconds. Among all the risk determinants (see Table 3), only atrial fibrillation longer than 6 months preoperatively was associated with a decreased probability of sinus rhythm restoration (78.1% versus 100%; $p = 0.05$). The isolated left atrium went on fibrillating in 48 patients (55.8%) (Fig 2A), showed an intrinsic rhythmic activity in 27 cases (32.5%) (Fig 2B), and showed no detectable electrical activity in 11 (12.7%) (Fig 2C).

Follow-up information has been gathered on all patients, and spans from 2 to 28 months (mean, 14.6 months). There were three late deaths: 1 case of unexplained sudden death (3 months postoperatively), 1 case of acute heart failure due to prosthetic valve detachment (3 months postoperatively), and 1 case of pneumonia (2 months postoperatively). Late complications consisted of endocarditis, defined as postoperative fever with positive blood cultures (5 patients, 2 of whom required prosthetic valve replacement), cerebral embolism (3 patients), and aortic prosthetic valve thrombosis, mitral valve incompetence, heart failure, and atrioventricular node reentry tachycardia (1 patient each).

Sinus rhythm persisted in 70 patients who survived the hospital period (72.1%): 44 patients in group I (71%), 11 patients in group II (61.2%), 12 patients in group III (85.8%), and 3 patients in group IV (100%) (Table 4; Fig 3).

The only determinant that was found to be associated with recurrence of atrial fibrillation was preoperative atrial fibrillation for longer than 6 months (see Table 4). Among the patients who were in sinus rhythm, mean atrioventricular conduction was 200 milliseconds; it was less than 200 milliseconds in 45 patients (75%), between 210 and 250 milliseconds in 12 (20%), and more than 250 milliseconds in 3 (5%).

Comment

Left atrial isolation was originally described as a technique for the control of atrial tachycardia [19–21]. The isolated left atrium often becomes asystolic or maintains an intrinsic slow rate; however, the presence of a right atrial "booster" function creates a satisfactory right heart output, and cardiac output can accordingly be maintained, the left ventricular being passively filled [19].

The experience with the epicardial approach in the surgical treatment of Wolff-Parkinson-White syndrome has taught that placement of cryolesions close to the valvular annuli does not impair the integrity of arteries of the atrioventricular junction or the strength of the mitral valve annulus itself [22].

With these premises, we decided to perform left atrial isolation in association with mitral valve operation in patients with long-standing atrial fibrillation.

Left atrial isolation is a simple additional procedure that can be performed by extending the left paraseptal atriotomy that is customarily used for the approach to the mitral valve. A minimal prolongation of the cross-clamping time is required, but the contemporary use of two cryoprobes reduces this time supplement.

The effectiveness of the left atrial isolation can be easily tested evaluating the absence of ventricular response after left atrial pacing (Fig 4). This test does not require any specific electrophysiological equipment, and therefore can be performed in any cardiac surgical unit.

Electrical isolation of the left atrium was obtained in a high percentage of patients (88%). In our experience with biatrial isolation ("corridor" procedure) for the treatment of idiopathic atrial fibrillation, we observed that failure in left atrial isolation was mainly due to persistence of conducting fibers along the external side of the coronary sinus. Significant improvement was obtained when we added a supplementary cryoablation at that site.

Long-term results show that freedom from atrial fibrillation can be obtained in a satisfactory percentage of patients (72%). Although patients with tricuspid valve incompetence who require a tricuspid valve annuloplasty had a higher recurrence rate of atrial fibrillation, this did not reach statistical significance. Only preoperative atrial fibrillation longer than 6 months was a significant risk factor for recurrence or persistence of atrial fibrillation.

The risk of postoperative thromboembolism is not decreased by the procedure, as the isolated left atrium can be fibrillating or electrically silent; because of this we customarily administer warfarin to those patients who undergo mitral valve repair.

Sinoatrial node function was satisfactory in all patients who gained sinus rhythm postoperatively; this fact suggests that long periods of atrial fibrillation do not necessarily carry the risk of definite damage of the natural pacemaker properties of the sinoatrial structures.

It is notable that of 91 patients with chronic atrial fibrillation who underwent mitral valve procedures without left atrial isolation in the same period, atrial fibrillation persisted in 73 (80.2%; unpublished data). Although the patients were not randomly assigned to the two surgical options, it is evident that recovery of the sinus rhythm was extremely more frequent in patients who underwent left atrial isolation than in those who did not (72% versus 19.8%; $p < 0.001$).

We conclude that the possibility of restoring and maintaining sinus rhythm in a high percentage of patients with long-standing atrial fibrillation secondary to rheumatic mitral, aortic, or mitral and aortic valve disease justifies the performance of left atrial isolation in association with mitral valve surgical procedures.

References

1. Papazoglou NM. Atrial fibrillation and mitral stenosis. Circulation 1974;49:1020–1.
2. Shimada S. A 13-year follow-up study of rheumatic valvular diseases. Jpn Circ J 1986;50:1304–8.
3. Tresch DD, Doyle TP, Bonchek LI, et al. Mitral valve prolapse requiring surgery. Clinical and pathologic study. Am J Med 1985;78:245–50.
4. Unverferth DV, Fertel RH, Unverferth BJ, Leier CL. Atrial fibrillation in mitral stenosis: histologic, hemodynamic, and metabolic factors. Int J Cardiol 1984;5:143–52.
5. Henry WL, Morganroth J, Pearlman AS, et al. Relation between echocardiographically determined left atrial size and atrial fibrillation. Circulation 1976;53:273–9.
6. Sanfilippo AJ, Abascal VM, Sheehan M, et al. Atrial enlargement as a consequence of atrial fibrillation. A prospective echocardiographic study. Circulation 1990;82:792–7.
7. Boyden PA, Tilley LP, Pham TD, Liu S, Fenoglio JJ, Wit AL. Effects of left atrial enlargement on atrial transmembrane potentials and structure in dogs with mitral valve fibrosis. Am J Cardiol 1982;49:1896–908.
8. Ten Eick RE, Singer DH. Electrophysiological properties of diseased human atrium. I. Low diastolic potential and altered cellular response to potassium. Circ Res 1979;44:545–57.
9. Herdorf AJ, Edie R, Malm JR, Hoffman BF, Rosen MR. Electrophysiologic properties and responses to pharmacologic agents of fibers from diseased human atria. Circulation 1976;54:775–9.
10. Cosio FG, Palacios J, Vidal JM, Cocina EG, Gomez-Sanchez MA, Tamargo L. Electrophysiologic studies in atrial fibrillation. Slow conduction of premature impulses: a possible manifestation of the background for reentry. Am J Cardiol 1983;51:122–30.
11. Probst P, Golshlager N, Selzer A. Left atrial size and atrial fibrillation in mitral stenosis. Circulation 1973;48:1282–7.
12. Selzer A, Kelly JJ, Gerbode F, et al. Treatment of atrial fibrillation after surgical repair of the mitral valve. Ann Intern Med 1965;62:1213–22.
13. Yang SS, Maranhao V, Monheit R, Ablaza SGG, Goldberg H. Cardioversion following open-heart valvular surgery. Br Heart J 1966;28:309–15.
14. Kahn DR, Kirsh MM, Ferguson PW, Sloan HE. Cardioversion after mitral valve operations. Circulation 1966;33(Suppl 3):138.
15. Sato S, Hirose H, Nakano S, et al. Follow-up study of atrial fibrillation associated with mitral stenosis after D-C cardioversion following open mitral commissurotomy. Nippon Geka Gakkai Zasshi 1986;87:1491–7.
16. Flugelman MY, Hasin Y, Katznelson N, Kriwiwsky M, Shefer A, Gotsman MS. Restoration and maintenance of sinus rhythm after mitral valve surgery for mitral stenosis. Am J Cardiol 1984;54:617–9.
17. Sato S, Hirose H, Nakano S, et al. Can atrial fibrillation be reverted to sinus rhythm after open commissurotomy for mitral stenosis? Actuarial maintenance rate of sinus rhythm at ten years after surgery. Kokyu To Junkan 1988;36:869–72.
18. Canas M, Rosselot I, Bahamonde L, Rosselot E. Cardioversion electrica en el postoperatorio de cirugia valvular mitral. Rev Med Chil 1986;114:632–5.
19. Williams JM, Ungerleider RM, Lofland GK, Cox JL. Left atrial isolation. New technique for the treatment of supraventricular arrhythmias. J Thorac Cardiovasc Surg 1980;80:373–80.
20. Chang JP, Chang CH, Yeh SJ, Yamamoto T, Wu D. Surgical cure of automatic atrial tachycardia by partial left atrial isolation. Ann Thorac Surg 1990;49:466–8.
21. Anderson KP, Stinson EB, Mason JW. Surgical exclusion of focal paroxysmal atrial tachycardia. Am J Cardiol 1982;49:869–74.
22. Guiraudon GM, Klein GJ, Sharma AD, Milstein S, McLellan DG. Closed-heart technique for Wolff-Parkinson-White syndrome: further experience and potential limitations. Ann Thorac Surg 1986;42:651–7.

DISCUSSION

DR D. CRAIG MILLER (Stanford, CA): Thank you, Dr Graffigna. This is a provocative report. Your procedure is almost a stripped-down Italian Ferrari version of the Cox procedure, isn't it?

DR GRAFFIGNA: Well, there are several differences between our procedure and Dr Cox's procedure. There is something similar in the consciousness that atrial fibrillation has a very complex mechanism and no direct procedure can be performed for its cure. But the Cox procedure, which is the "maze" operation, actually aims at the creation of blind alleys along which the atrial activation spins from the right to the left atrium. Left atrial isolation is designed to frame the fibrillating activity within the left atrium or, as an alternative mechanism—the concepts are still not clear—to reduce the atrial surface and therefore the probability of development of postoperative atrial fibrillation. This is the concept of the corridor procedure, let us say.

DR MILLER: So you would not expect your procedure to be as effective as the "maze" operation in terms of atrial pump transport function or reduction of systemic emboli?

DR GRAFFIGNA: In terms of atrial transport, there is a great deal of experimental work of the early 1980s stating that the presence of at least one atrial cavity synchronous with the corresponding ventricle still exerts its booster function, so that the cardiac output of that side of the heart is increased. In the case of the left atrial isolation procedure, the right atrium would perform a booster function on the right ventricle and right ventricular cardiac output would be incremented, while the left ventricle would be passively filled.

MR ENDRE BODNAR (Pinner, UK): It is not an extreme rarity to see a large left atrium in electrical sinus rhythm but without any mechanically effective atrial contraction. I am impressed by the electrocardiogram you showed us, but do you have any evidence that you restored the mechanical activity of the left atrium?

DR GRAFFIGNA: The fact is that the mechanical activity of the left atrium is not expected. We expect to restore the mechanical activity of the right atrium.

MR BODNAR: If you do not restore the mechanical activity of the left atrium, you do not decrease the thromboembolic danger. What, then, is the rationale for the left atrial isolation?

DR GRAFFIGNA: The procedure is not specifically directed to the reduction of the thromboembolic risk. The thromboembolic risk remains that of a patient who has atrial fibrillation and undergoes mitral prosthetic valve implantation. The possibility of reducing the thromboembolic risk by means of warfarin is typically established. The actual difficulty is the clinical evaluation of the hemodynamic advantage of this procedure, in that it could be technically difficult to evaluate the cardiac output of these patients in sinus rhythm or after induction of atrial fibrillation.

MR BODNAR: Recent clinical experience shows that when those large left atria without mechanical contraction go into atrial fibrillation, or back into sinus rhythm, there is no change whatsoever regarding embolic risk. The electric sinus rhythm does not matter, if the atrium does not contract.

DR TIRONE E. DAVID (Toronto, Ont, Canada): I enjoyed your report very much. I think this is a good idea. I am not sure how effective this procedure is, but I promise you I am going to try it.

Why do you use a cryoprobe? Why don't you simply cut all around the left atrium, isolating it from the mitral valve? Wouldn't you accomplish the same thing? It would be a simpler operation.

DR GRAFFIGNA: Well, I think that technically that might imply a longer left atrial incision, and it would also imply a greater risk for the vascular structures of the atrioventricular fat pad. We prefer the closure cryoablations to limit the extent of the left atrial incision without making a circumferential exclusion of the cavity. But if you say that you are stimulated by our experience, that is the principal aim of this presentation.

DR DAVID: I do not have the numbers of patients we have operated on; however, particularly when we repair the mitral valve we make a very generous atriotomy, 1 or 2 cm from the left atrial appendage orifice to the level immediately below the midportion of the posterior leaflet of the mitral valve. I believe that at least one-half of our patients who had atrial fibrillation before operation went back into sinus rhythm afterward. So, if you had a 75% rate of return of sinus rhythm, one should ask how much this restoration of sinus rhythm was due to the incision and cryoablation you made and how much was due to correction of the valve dysfunction.

DR GRAFFIGNA: The observation is intriguing. As you probably saw in a previous slide, we have a personal experience in patients with atrial fibrillation undergoing mitral valve operation alone. Sinus rhythm was recovered in the long term in only 19% of such patients. And although this is not a double-blind comparison, these results led us to think that the left atrial isolation procedure increases the recovery of the sinus rhythm up to 75%.

Combined Carotid and Coronary Revascularization: The Preferred Approach to the Severe Vasculopath

Robert J. Rizzo, MD, Anthony D. Whittemore, MD, Gregory S. Couper, MD, Magruder C. Donaldson, MD, Sary F. Aranki, MD, John J. Collins, Jr, MD, John A. Mannick, MD, and Lawrence H. Cohn, MD

Department of Surgery, Harvard Medical School, and Divisions of Cardiac and Vascular Surgery, Brigham and Women's Hospital, Boston, Massachusetts

The timing of carotid endarterectomy (CEA) and coronary revascularization (CABG) for concomitant disease is controversial. Results of combined CEA/CABG in 127 patients (age range, 46 to 82 years; mean age, 65 years; 61% male) from 1978 to 1991 were reviewed. Ninety-five patients (75%) were in New York Heart Association functional class III or IV, 48 (38%) had left main coronary artery disease, and 32 (28%) had depressed ejection fraction (<0.50). Forty (32%) had asymptomatic bruits, 61 (48%) transient ischemic attacks, and 26 (20%) prior strokes. Seventy-five (59%) had bilateral carotid stenosis, including 20 (16%) with contralateral occlusions. Perioperative mortality was 7 of 127 (5.5%), and all deaths were cardiac related. Myocardial infarctions occurred in 6 of 127 patients (4.7%) and were nonfatal in 3 (2.3%). Permanent strokes occurred in 7 of 127 (5.5%) and were ipsilateral in 5 (3.9%). Perioperative stroke did not occur in the asymptomatic group, but the risk was higher in those with prior stroke (19%) or with contralateral carotid occlusion (15%). The stroke risk for our patients with carotid disease having CABG without CEA is not known, but the literature reports rates as high as 14%. For our patients without known concomitant disease, the risk of permanent stroke was 1.0% (31/3012) for isolated CABG and 1.5% (7/482) for isolated CEA. The late results after CEA/CABG revealed a 5-year survival of 70% ± 5%, which correlated with ejection fraction (≥0.50, 81% ± 5%; <0.50, 45% ± 11%; $p < 0.003$). Freedom from late permanent ipsilateral stroke was 97% ± 2% at 8 years. Freedom from stroke at 5 years was lower among patients with a previous stroke (71% ± 10%) compared with transiently symptomatic (90% ± 4%) and asymptomatic (96% ± 4%) patients ($p < 0.03$). Combined CEA/CABG is a useful option in this high-risk group of patients with extensive atherosclerosis; avoids a subsequent hospitalization, anesthetic, and delay period; and provides long-term protection from ipsilateral stroke.

(Ann Thorac Surg 1992;54:1099–109)

Patients with severe concomitant carotid and coronary atherosclerosis represent a difficult, high-risk population, and controversy still exists regarding the optimal method of surgical management of their multisystem atherosclerotic disease. Carotid endarterectomy (CEA) in the setting of severe uncorrected coronary disease has been associated with an operative mortality rate as high as 20%, primarily due to myocardial infarction [1, 2]. Likewise, coronary revascularization (CABG) in the presence of severe carotid disease is associated with up to a 14% risk of perioperative stroke [3]. Bernhard and associates [1] first proposed combined carotid endarterectomy and coronary revascularization in 1972 as an effective means to reduce operative mortality and morbidity in patients with concomitant carotid and coronary disease. Since then, many studies using multiple techniques have been reported that attempt to support or refute the concept of simultaneous revascularization, yet few report the operative and late results of the combined approach [4–11].

The present study reviews the early and late cardiac and neurologic results of combined CEA and CABG at the Brigham and Women's Hospital in Boston during the past 13 years. These results are compared with those of isolated CEA and CABG in patients without known concomitant disease at this hospital. In addition, the results of patients with combined disease managed by either isolated CABG or combined CEA and CABG as reported in the literature are reviewed.

Material and Methods

Patients

From January 1, 1978 to December 30, 1991, 127 patients (77 male or 61%, 50 female or 39%) aged 46 to 82 years (mean age, 65 years) underwent combined CEA and CABG for severe cerebrovascular disease and coronary artery disease (CAD). Preoperative clinical data are summarized in Table 1. From a neurologic standpoint, 40 patients (32%) were asymptomatic and 87 (68%) were symptomatic, including 61 with transient symptoms and 26 with prior cerebrovascular accidents (CVAs). Transient symptoms included transient ischemic attacks (TIAs) or amaurosis fugax in 57 patients and syncope in 4. Patients underwent carotid evaluation before CABG on a selective and not routine basis dependent on clinical stability and

---

Presented at the Twenty-eighth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Feb 3–5, 1992.

Address reprint requests to Dr Rizzo, Division of Cardiac Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Characteristics of the CEA/CABG, Isolated CABG, and Isolated CEA Group

Characteristic	CEA/CABG (n = 127)	Isolated CABG (n = 3,012)	p Value[a]	Isolated CEA (n = 482)	p Value[a]
Female	50 (39%)	809 (27%)	0.002	180 (37%)	0.39
Age ≥70 years	35 (28%)	953 (32%)	0.19		
Family Hx of CAD	84 (66%)	1,632 (54%)	0.005		
Hypertension	94 (74%)	1,902 (63%)	0.007	283 (59%)	0.001
Diabetes	42 (33%)	835 (28%)	0.11	88 (18%)	0.0004
History of MI	85 (67%)	1,850 (61%)	0.12		
Smoker	103 (81%)	1,346 (45%)	<0.0001	232 (48%)	<0.0001
EF <0.50	32 (28%)	661 (31%)	0.30		
LM ≥50%	48 (38%)	693 (23%)	0.0002		
Preop IABP	6 (5%)	328 (11%)	0.01		
Cardiac symptoms					
CHF	4 (3%)	59 (2%)	0.57		
CHF + angina	32 (25%)	339 (22%)			
Stable angina	25 (20%)	587 (20%)			
Unstable angina	61 (48%)	1,623 (54%)			
Asymptomatic & ETT+	5 (4%)	74 (2%)			
Neurologic symptoms					
Asymptomatic	40 (31%)			143 (30%)	0.003
Transient symptoms	61 (48%)			307 (63%)	
Prior CVA	26 (20%)			32 (7%)	
NYHA			0.09		
I	8 (6%)	120 (4%)			
II	24 (19%)	559 (18%)			
III	40 (32%)	1,257 (42%)			
IV	55 (43%)	1,076 (36%)			
Circumstances			0.04		
Elective	84 (66%)	1,694 (56%)			
Urgent	41 (32%)	1,193 (40%)			
Emergent	2 (2%)	125 (4%)			
No. of Grafts			0.63		
1	3 (2%)	100 (3%)			
2	25 (20%)	506 (17%)			
3	53 (42%)	1,408 (47%)			
4	37 (29%)	847 (28%)			
5	9 (7%)	151 (5%)			

[a] p Values (Fishers's exact test or χ^2) test for difference between the CEA/CABG group and the isolated CEA and CABG groups.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CEA = carotid endarterectomy; CHF = congestive heart failure; CVA = cerebrovascular accident; EF = ejection fraction; ETT+ = positive exercise test; Hx = history; IABP = intraaortic balloon pump; LM = left main occlusion; MI = myocardial infarction; NYHA = New York Heart Association functional class.

the presence of a bruit or a history of neurologic symptoms consistent with carotid disease. Carotid disease was diagnosed by noninvasive ultrasound testing, angiography, or both and was considered serious when diameter was reduced by greater than 50%. Carotid stenosis was less than 70% in 4 patients (3%). Carotid disease was unilateral in 52 (41%) and bilateral in 75 (59%), including 20 (16%) with contralateral occlusion. In patients with bilateral disease, CEA was performed on the symptomatic side, or if the patients were asymptomatic, on the tighter side or that flowing to the dominant hemisphere.

Operative Technique

After placement of electrocardiographic and electroencephalographic leads, radial arterial line, and pulmonary arterial catheter, premedicated patients were anesthetized with the induction objectives of maintaining stable blood pressure, pulmonary capillary wedge pressure, and baseline electrocardiogram and then intubated. Carotid and cardiac surgical procedures were performed by two teams. Early in this experience and in patients in unstable condition, carotid exposure, median sternotomy, and cannulation were performed simultaneously. More recently, in patients in stable condition, carotid exposure and endarterectomy were performed while the saphenous vein was dissected from the leg before sternotomy. Anticoagulation with 5,000 units of heparin was used for the carotid endarterectomy. An indwelling carotid shunt was used routinely if an electroencephalogram was not available, or selectively if the electroencephalogram changed after carotid clamping. The electroencephalogram was used in 98 patients (77%), and changes in 17 (13%) necessitated the insertion of a shunt. Carotid shunts were used in 30 patients (24%), and in those without shunts the clamp time ranged from 15 to 65 minutes (mean, 32 minutes). The arteriotomy was closed primarily in most patients, but with a vein patch in 4 (3%). The neck wound was packed with iodophor-soaked gauze, and cardiopulmonary bypass was instituted. Moderate systemic hypothermia (28°C) was induced with bypass flows of 1.25 to 2.5 $L \cdot min^{-1} \cdot m^{-1}$. After the aorta was clamped, the heart was arrested with cold hyperkalemic cardioplegia and kept cool with continuous iced saline lavage. Coronary bypass conduits included internal mammary artery and reversed saphenous vein. The internal mammary artery was used in 46% of all patients (59/127), in 75% of those since 1983 (55/73), and in 93% of those since 1988 (25/27). Vein grafts were anastomosed distally first and then after aortic unclamping were anastomosed proximally to the aorta. After completion of coronary revascularization, extracorporeal circulation was discontinued and the chest and neck wounds were closed over drains. The aortic cross-clamp time ranged from 12 to 149 minutes (mean, 41 minutes) and the cardiopulmonary bypass time from 35 to 185 minutes (mean, 77 minutes).

Operative and late follow-up information was obtained by chart review and direct communication with patients and their families, primary physicians, and health authorities via mailings and the telephone. Follow-up information was obtained for 121 of the 127 patients. The effective sample size was 43 (34%) at 5 years and 19 (15%) at 8 years, and the mean follow-up was 3.9 years. A stroke was defined as any neurologic event consistent with a central source that required more than 24 hours for resolution. Strokes from which the patient fully recovered within 30 days were reported as transient; all others were considered permanent.

Statistical Methods

The characteristics of our CEA/CABG group were compared with those of the isolated CABG and the isolated CEA groups using Fisher's exact test and the χ^2 test [12]. Differences in the rates of the outcomes—operative death, myocardial infarction (MI), and stroke—were analyzed with Fisher's exact test. Freedom from late death, MI, and stroke in the CEA/CABG group was examined with actuarial (life-table) models and tested for differences among strata using the log-rank and Wilcoxon statistics [13]. Analyses were conducted in PC SAS (SAS Institute, Inc, Cary, NC).

Results

The clinical characteristics of the CEA/CABG group listed in Table 1 are compared with those of 3,012 patients having isolated CABG (1987 to 1991) and 480 patients having isolated CEA (1983 to 1991) during similar periods at this hospital. The CEA/CABG group had significantly more women and more patients with hypertension, smoking history, and left main CAD than the isolated CABG group but required fewer preoperative intraaortic balloon pumps. The CEA/CABG group had significantly more patients with hypertension, diabetes, and smoking history than the isolated CEA group.

Table 2. Perioperative and Late Events in 127 CEA/CABG Patients

Event	Perioperative	Late	Total
Death	7	34	41
MI	6	6	12
Reop CABG		5	5
Reop CEA			
Ipsilateral	1	0	1
Contralateral	0	7	7
Total	1	7	8
CVA (permanent/transient)			
Ipsilateral	5/1	2/1	7/2
Contralateral	2/0	2/0	4/0
Unknown		1/0	1/0
Total	7/1	5/1	12/2
TIA			
Ipsilateral	1	0	1
Contralateral	1	1	2
Total	2	1	3

CABG = coronary artery bypass grafting; CEA = carotid endarterectomy; MI = myocardial infarction; TIA = transient ischemic attack.

Perioperative and late events identified in the CEA/CABG population are listed in Table 2. There were seven perioperative deaths and all were cardiac related: three MIs, two arrhythmias, one low cardiac output state, and one mediastinal hemorrhage from a vein graft. Two of these deaths occurred in reoperation coronary bypass procedures, one in a patient with stenosed vein grafts and the other in a 48-year-old woman with diffuse CAD 15 and 21 years after bilateral Vineberg internal mammary artery implantations. There were three nonfatal perioperative MIs. There were eight perioperative strokes, one of which completely resolved within 30 days and was considered transient; the other seven persisted to at least a mild degree beyond 30 days and were considered permanent. Six of the perioperative strokes were ipsilateral to the CEA, including the transient stroke, whereas the two contralateral strokes occurred above contralateral carotid occlusions. All of the perioperative strokes were identified on the first postoperative day shortly after the patient awoke from anesthesia except one. In this case, the patient had already awakened and appeared neurologically intact when he suffered a cardiac arrest and after resuscitation was found to be hemiplegic. Noninvasive carotid evaluation revealed thrombosis of the CEA site, and the patient underwent emergent carotid thrombectomy and vein patch and gradually recovered. There were two perioperative TIAs which resolved well within 24 hours, one of which was ipsilateral to the CEA.

The late events identified in the CEA/CABG population include 34 deaths, 6 MIs, 5 reoperation CABGs, 6 CVAs (5 permanent and 1 transient), 1 TIA, and seven contralat-

Table 3. Perioperative Death, MI, and CVA Rates for CEA/CABG Versus Isolated CABG and Isolated CEA

Variable	Primary & Reop CEA/CABG 1978–1991	Isolated CABG 1987–1991	Isolated CEA 1983–1991
No. of patients	127	3012	482
Death	5.5%	4.0%	0.6%[a]
MI	4.7%	4.7%	0.8%[a]
CVA	6.3%	1.4%[a]	1.5%[a]
CVA—permanent	5.5%	1.0%[a]	1.5%[a]

[a] $p < 0.01$.

CABG = coronary artery bypass grafting; CEA = carotid endarterectomy; CVA = cerebrovascular accident; MI = myocardial infarction.

eral CEAs. The cause of the late deaths was cardiac in 17 patients, aortic dissection in 1, stroke in 2, renal failure in 3, cancer in 2, trauma in 1, and unknown or other in 8. Only three of the seven late ischemic neurologic events were known to be ipsilateral to the CEA, of which two were permanent CVAs including one that was fatal. Laterality in one late fatal CVA could not be determined.

The operative results of the CEA/CABG procedures on patients with combined disease are listed and compared with those of the isolated CABG and isolated CEA procedures on patients with isolated disease in Table 3. For the CEA/CABG group, the operative mortality was 5.5% and morbidity included MI, 4.7%; CVA, 6.3%; permanent CVA, 5.5%; and permanent ipsilateral CVA, 3.9%. The cumulative operative risk for the isolated CABG and isolated CEA procedures was 4.6% for death, 5.5% for MI, 2.9% for CVA, and 2.5% for permanent CVA. The preoperative neurologic symptoms, severity of disease, and operative factors for the CEA/CABG group are listed and correlated with their respective perioperative and late risk of CVA in Table 4.

A perioperative CVA occurred in 42 of 3,012 isolated primary CABG operations, and carotid studies were obtained postoperatively in 31 of these patients. Unsuspected carotid disease was found in 29% (12/42) of all patients who suffered strokes after CABG without having preoperatively known carotid disease. The unsuspected carotid disease appeared to be the most likely cause of the CVA in 24% (10/42) of these patients, and total carotid occlusion was present in only 2 of these 12 patients with serious carotid disease.

In the CEA/CABG group, the overall 5-year survival was 70% ± 5%. Freedom at 5 years from MI was 84% ± 4%, and freedom at 5 years from all CVA was 88% ± 3%. A significant difference ($p < 0.003$) in survival was observed between patients with preserved ejection fraction (81% ± 5% at 5 years) and decreased ejection fraction (45% ± 11% at 5 years) as depicted in Figure 1. Regarding stroke, the difference in 5-year freedom from all perioperative or late (88% ± 3%), late only (95% ± 2%), and late permanent ipsilateral (97% ± 2%) stroke is illustrated in Figure 2A. When survival to stroke was evaluated based on preoperative symptoms, a significant difference ($p < 0.03$) in freedom from all stroke at 5 years was observed between patients who were preoperatively asymptomatic (96% ± 4%), were transiently symptomatic (90% ± 4%), or had prior CVA (71% ± 10%), as illustrated in Figure 2B. Although patients with contralateral occlusion had a high (3 of 20, or 15%) early stroke risk, there were no late strokes in this group and thus there was no significant difference in freedom from all strokes based on the pathologic severity of carotid disease.

Table 4. Cerebrovascular Risk Factors and Perioperative or Late CVA in 127 CEA/CABG Patients

Variable	Total	Perioperative		Late	
		CVA	Ipsilateral CVA	CVA	Ipsilateral CVA
Symptoms					
Asymptomatic	40 (32%)	0 (0.0%)	0	2 (5%)	1
Symptomatic	87 (68%)	8 (9.2%)	6	4 (4.6%)	2
Transient	61 (48%)	3 (4.9%)	2	3 (4.9%)	1
Prior CVA	26 (20%)	5 (19.2%)	4	1 (3.8%)	1
Carotid disease					
Unilateral	52 (41%)	4 (8%)	4	4 (7.7%)	3
Bilateral	75 (59%)	4 (5%)	2	2 (2.7%)	0
Without contralateral occlusion	55 (44%)	1 (2%)	1	2 (3.6%)	0
With contralateral occlusion	20 (16%)	3 (15%)	1	0 (0.0%)	0
Operative factors					
EEG unchanged	81 (64%)	4 (5%)			
EEG changed	17 (13%)	4 (24%)			
EEG not available	29 (23%)	0 (0%)			
Shunt	30 (24%)	3 (10%)			

CVA = cerebrovascular accident; EEG = electroencephalogram.

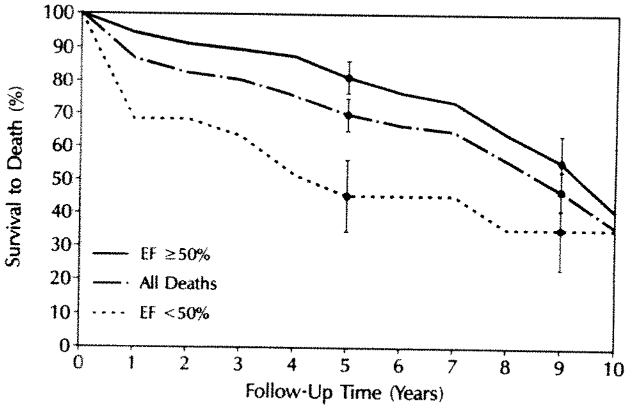


Fig 1. Actuarial survival to perioperative or late death in the carotid endarterectomy/coronary artery bypass grafting group for all patients and those with ejection fraction (EF) ≥0.50 (50%) and <0.50. A significant difference in survival was observed between patients with preserved and depressed EF (p < 0.003).

Comment

Patients with concomitant severe carotid and coronary disease are, in general, a much higher risk population than patients with isolated carotid or coronary atherosclerotic disease. In this CEA/CABG series, the percentage of patients with atherosclerotic risk factors such as hypertension, diabetes, and a history of smoking was significantly increased compared with patients undergoing isolated CEA or CABG procedures. In addition, the CEA/CABG population had a greater percentage of women and patients with severe left main CAD than the isolated CABG group, and these were factors associated with an increased operative mortality risk within the isolated CABG group (overall, 4%; women, 6.6%; left main CAD, 5.2%). The greater percentage of elective cases within the CEA/CABG group probably reflects the increased time taken to assess the carotid arteries, establish a diagnosis, and schedule a convenient time for both the vascular and cardiac teams to perform the combined procedure. The mortality rate of 5.5% for CEA/CABG includes two deaths in reoperative CABG procedures. The mortality rate for primary CEA/CABG was 4.3%, which is similar to the mortality of 4% for the primary isolated CABG group. The primary CEA/CABG operative mortality (4.3%) and MI (4.7%) rates were actually slightly lower than the cumulative mortality (4.6%) and MI (5.5%) rates for the isolated CABG and isolated CEA procedures. The low operative mortality (0.6%) and MI (0.8%) rates in the isolated CEA population are likely reflective of the preference in our hospital to avoid isolated CEA in the presence of severe CAD.

The 5-year survival in this CEA/CABG group was 70% ± 5%, slightly lower than reported in other series of CEA/CABG (74% to 86%) [4, 6–9]. Hertzer and associates [6] observed a decreased 5-year survival after CEA/CABG (81%) relative to isolated CABG (92%). Patients in our CEA/CABG group with decreased ejection fraction had significantly worse 5-year survival (45% ± 11%) than those with preserved left ventricular function (81% ± 5%). A similar difference in survival after isolated CABG based on left ventricular function has been observed in larger studies, including one by Hoffman and colleagues [14] (normal ejection fraction, 92%; poor ejection fraction, 70%). Patients with combined disease requiring combined CEA/CABG appear to have decreased long-term survival in comparison with patients with isolated coronary disease. This is likely a reflection of the diffuse and severe nature of the atherosclerotic disease in the CEA/CABG group.

The presence of severe carotid disease is the most obvious reason for the increased overall stroke rate in the CEA/CABG patients (6.3%) compared with the isolated CABG group (1.4%), and this increased stroke rate was noted across almost all demographic categories. Another reason for the increased stroke rate in the CEA/CABG group with known multisegment atherosclerotic disease may be an associated increased rate of ascending aortic

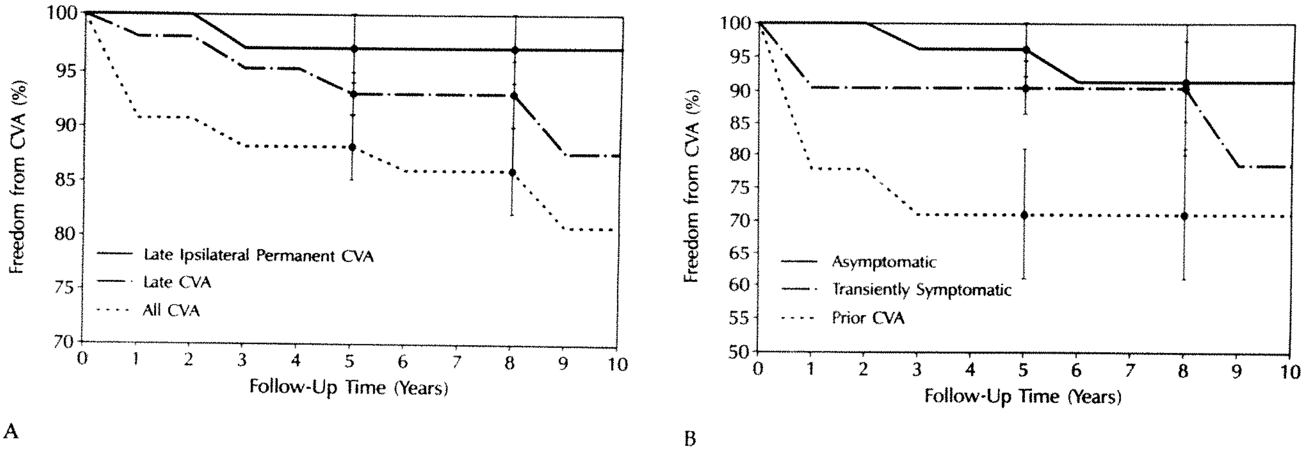


Fig 2. Actuarial freedom from perioperative or late stroke in the carotid endarterectomy/coronary artery bypass grafting group. (A) All perioperative or late cerebrovascular accidents (CVA), late CVA, and late permanent ipsilateral CVA. (B) All perioperative or late CVA based on preoperative neurologic symptoms. Survival was different between patients who were asymptomatic, transiently symptomatic, or had a prior CVA (p < 0.03).

disease, which may embolize secondary to cannulation, clamping, and construction of the proximal vein graft anastomoses. In a recent pathologic study, ulcerated plaques were identified within the ascending aorta or arch in 26% of 239 patients with evidence of stroke and in 61% of those with no known cause of stroke [15]. All but one of the strokes in the CEA/CABG group were apparent once the patient awakened, suggesting an intraoperative cause for most of the strokes. These could be explained by embolization from the carotid plaque, endarterectomy site, aortic disease, or heart, or inadequate cerebral perfusion ipsilaterally during carotid clamping or contralaterally above occlusive disease during carotid clamping or cardiopulmonary bypass. Two of the seven intraoperative strokes occurred above contralateral occlusions and two were associated with electroencephalographic changes during carotid clamping. The remaining three were not associated with either of these hypoperfusion scenarios and we therefore suspect embolization as their cause. One of these 3 patients had a stroke preoperatively as a complication of cardiac catheterization, suggesting a cardiac or aortic source for embolization. Aortic disease may be more common in patients with carotid and coronary atherosclerotic disease and may help explain their elevated stroke risk, though proof of this correlation is lacking.

Jones and co-workers [16] also reported an increased stroke rate in a series of combined CEA/CABG operations (1.6%) versus primary CABG operations (0.6%) without known carotid disease and emphasized the importance of aortic atherosclerotic embolization in the etiology of stroke after CABG. Gardner and associates [17] identified several stroke risk factors in patients undergoing isolated CABG. These included increased age, cerebrovascular disease, ascending aortic atherosclerosis, protracted cardiopulmonary bypass time, and severe perioperative hypotension. In reviewing the 42 strokes that occurred after primary CABG in our hospital since 1987, it was enlightening to note that serious carotid disease was subsequently identified in 29% of the total and 39% (12/31) of the patients in whom the carotids were studied. Because total carotid occlusion was present in only 2 of the 12 patients in whom carotid disease was identified, most of these patients (83%) had disease potentially correctable by CEA. In patients with carotid occlusions and perhaps in all patients with cerebrovascular disease, it may be helpful to include computerized electroencephalographic monitoring to document cerebral hypoperfusion, which may be corrected by increasing perfusion pressure or carbon dioxide tension as described by Arom and colleagues [18]. The common finding of carotid disease in patients with CVA after CABG implies that carotid disease plays a major role in the etiology of stroke after CABG even when not clinically suspected, or that the presence of carotid disease in patients with CAD is an indicator that other risks are present, such as severe aortic disease.

Whether it is necessary to screen the carotids of all patients having CABG is controversial and dependent on the incidence of disease and the usefulness of knowing this information. Reports of routine carotid evaluation before CABG have documented serious carotid stenosis in 2.8% to 11.8% of patients [3, 5, 6, 19, 20]. Although preoperative evaluation of all CABG patients has not been routine at our hospital, the minimum incidence of major carotid disease in our CABG population can be estimated. Since 1987, carotid disease was documented postoperatively in 12 of the 42 patients who suffered a perioperative stroke among the 3,012 isolated CABG patients and preoperatively in the 40 patients who had a CEA/CABG, for a total minimum incidence of 1.7%: (12 + 40)/(3,012 + 40). This estimation does not include the unknown number of patients having isolated CABG who may have had carotid disease but were not studied preoperatively for lack of symptoms, bruit, or adequate time and did not suffer a perioperative CVA, thus avoiding a postoperative examination. Faggioli and associates [3] recently found major carotid disease (>75% stenosis) in 11% of patients more than 60 years of age screened before CABG. If CEA is proven beneficial for asymptomatic carotid disease, as an ongoing clinical trial suggests [21], then screening of populations at high risk for carotid disease may be worthwhile.

The preoperative neurologic symptoms in the CEA/CABG group correlated with perioperative stroke risk. The highest risk category, prior CVA, was more common in the CEA/CABG group than in the isolated CEA group. Whereas none of the asymptomatic patients sustained a CVA, 9% of all of the symptomatic patients and 19% of the patients with prior CVAs had a new CVA. Hertzer and associates [6] reported a 20% new neurologic deficit rate in patients having prior strokes and undergoing CEA/CABG. The other high-risk group in the present study included patients with bilateral carotid disease with contralateral carotid occlusion (15% CVA). Brener and co-workers [5] also demonstrated, in a small number of patients having CABG in the presence of bilateral carotid disease with contralateral occlusion, that these patients are at high risk for perioperative stroke after CABG, whether performed as a CEA/CABG (3 of 7 or 43%) or as an isolated CABG (1 of 5 or 20%). Randomized studies comparing approaches to these very high risk groups may be necessary to be able to select the approach associated with the least risk of perioperative stroke. However, the recent North American Symptomatic Carotid Endarterectomy Trial does strongly support the effectiveness of CEA in reducing the overall risk of stroke in symptomatic patients with 70% or greater carotid stenosis (8% with CEA versus 27% without CEA at 18 months) [22].

The permanent stroke risk for the CEA/CABG procedures (5.5%) in patients with combined carotid and coronary disease in this study was roughly twice the cumulative stroke risk (2.5%) for the isolated CABG (1.0%) and isolated CEA procedures (1.5%) in patients with isolated disease. A similar difference in stroke rate was reported by Cambria and associates [23] in patients undergoing combined CEA/CABG (4.2%) versus those having isolated CABG (0.6%) without carotid disease and isolated CEA (1%) added together (1.6%). The stroke risk for patients with combined carotid and coronary disease undergoing simultaneous CEA/CABG appears to be more than the

Table 5. Combined Carotid and Coronary Revascularization Studies of 50 or More Patients: Perioperative Events (≤1 month)

Reference	Year	No. of Patients	Mean Age (y)	Neurologic Symptoms (%)	Bilateral Disease (%)	Left Main (%)	Reop CABG (%)	Death (%)	MI (%)	CVA (%)	Perm CVA (%)
Ennix et al [2]	1979	51	?	?	?	?	?	5.9	5.9	0	0
Rice et al [24]	1980	54	?	48	4	4	?	0	0	3.8	1.9
Schwartz et al [25]	1982	73	62	44	60	37	?	9.6	0	2.7	1.4
Hertzer et al [4]	1983	331	61	48	35	21	?	5.7	6.3	9.0	4.5
Jones et al [16]	1984	132	62	33	51	15	?	3.0	0.8	1.6	1.6
Babu et al [26]	1985	62	?	45	30	?	?	4.8	0	4.8	1.6
Reul et al [27]	1986	143	?	82	?	?	?	4.0	?	2.8	2.8
Dunn et al [28]	1986	130	60	20	40	12	4	4.6	?	10.0	3.8
Brener et al [5]	1987	57	?	0	39	?	?	10.5	?	8.8	1.8
Perler et al [29]	1988	61	62	52	48	34	8	11.5	3.2	3.2	3.2
Hertzer et al [6]	1989	170	65	58	58	24	7	5.3	?	7.1	5.3
Minami et al [30]	1989	116	69	43	?	?	?	1.7	1.7	4.3	1.7
Duchateau et al [7]	1989	82	60	36	40	30	?	7.3	0	4.9	3.7
Cambria et al [23]	1989	71	65	31	46	37	?	2.8	2.8	4.2	4.2
Pome et al [8]	1991	52	61	44	44	13	8	0	7.7	1.9	0
Vermeulen et al [9]	1992	230	63	47	40	29	7	3.5	1.8	6.1	3.0
Total		1,815						4.8	3.0	5.6	3.1
Range		51–331	60–69	0–82	4–60	4–37	0–8	0–11.5	0–7.7	0–10	0–5.3
Present series	1992	127	65	68	59	37	9	5.5	4.7	6.3	5.5

CABG = coronary artery bypass grafting; CVA = cerebrovascular accident; MI = myocardial infarction; Perm = permanent.

additive risks of patients with isolated disease undergoing isolated CEA and isolated CABG. This increased stroke risk, as with the decreased long-term survival, appears related to the overall severity of atherosclerotic disease in these patients with advanced, diffuse, and multisystemic involvement.

A review of the literature of combined carotid and coronary revascularization in studies of 50 or more patients is listed in Table 5 [2, 4–9, 16, 23–30]. These studies include populations with a wide range of cardiac and neurologic risk factors, but the overall estimated operative risk of mortality was 4.8%, that of MI was 3.0%, and that of permanent CVA was 3.1%. The risks in the present series fall within the ranges reported for mortality and MI, and lie just above the range of CVA. However, carotid disease was frequently symptomatic or bilateral in our series, as it was in the latest series from the Cleveland Clinic [6], and the risk of CVA was very similar (5.5% to 5.3%) in these comparable groups. Several reports of the risk of late CVA after CEA/CABG for both asymptomatic and symptomatic carotid disease are summarized in Table 6. Among the combined total of 919 patients in these studies with a mean follow up of 26 to 35 months, 4.8% had a late CVA but only 1.3% suffered a CVA ipsilateral to the CEA.

A summary of reports of CABG performed in the presence of diagnosed but uncorrected carotid disease is presented in Table 7 [1, 3, 5, 6, 16, 19, 31–38]. Once again, these studies represent populations with a wide variety of demographic features, but the overall risk of permanent

Table 6. Combined Carotid and Coronary Revascularization Studies of 50 or More Patients: Late Events (>1 month)

Reference	Year	No. of Patients	Mean Follow-up (mo)	Neurologic Symptoms (%)	Bilateral Disease (%)	TIA (%)	CVA (%)	PI CVA (%)
Hertzer et al [4]	1983	312	30	48	35	?	5.8	1.6
Hertzer et al [6]	1989	257	26	58	58	?	2.3	0.4
Duchateau et al [7]	1989	76	29	36	39	1.3	2.6	0.0
Pome et al [8]	1991	52	35	44	44	9.6	1.9	0.0
Vermeulen et al [9]	1992	222	?	47	40	6.3	7.7	2.7
Total		919				5.7	4.8	1.3
Range		52–312	26–35	36–58	39–58	0–9.6	1.9–7.7	0–2.7
Present series	1992	120	46	68	59	0.8	4.2	1.7

CVA = cerebrovascular accident; PI = permanent ipsilateral; TIA = transient ischemic attack.

Table 7. CABG With Unoperated Major Carotid Disease: Perioperative Events (≤1 month)

Reference	Year	No. of Patients	Operation	Symptoms No	Symptoms Yes	Diagnostic Study	Bilateral Disease (%)	Death (%)	CVA (%)	Permanent CVA (%)
Ennix et al [2]	1979	84	CPB	40	44	Angio	38	?	2.4	2.4
Turnipseed et al [19]	1980	20	CPB	Mixed		Noninvasive	?	?	10	10.0
Barnes et al [31]	1981	40	CPB	40	0	Noninvasive	?	10	2.5	2.5
Breslau et al [32]	1981	5	CPB	5	0	Noninvasive	0	?	0	0
Kartchner et al [33]	1982	41	CPB/VAS	Mixed		Noninvasive	?	?	17	17
Ogren et al [34]	1983	20	CPB	20	0	Noninvasive	?	?	5	5
Jones et al [16]	1984	130	CPB	60	70	Angio 40%	23	?	6	6
Ivey et al [35]	1984	16	CPB	16	0	Noninvasive	?	?	4	0
Furtan et al [36]	1985	29	CPB	Mixed		Angio	23	?	3.4	3.4
Brener et al [5]	1987	64	CPB	64	0	Noninv/Angio	23	16	7.8	3.1
Schultz et al [37]	1988	50	CPB	50	0	Noninvasive	?	7	0	0
Hertzer et al [6]	1989	81	CPB	58	23	Angio	40	3	7.4	7.4
Faggioli et al [3]	1990	28	CPB	28	0	Noninvasive	?	?	14.3	14.3
Johnsson et al [38]	1991	7	CPB	3	4	Noninvasive	100	?	0	0
Total		615							6.0	5.5
Range		5–130					0–100	3–16	0–17	0–17
Total–CPB only		574							5.2	4.7
Asymptomatic		344							4.9	4.1
Symptomatic		97							8.2	8.2

CPB = cardiopulmonary bypass; CVA = cerebrovascular accident; VAS = vascular.

stroke ranged from 0% to 17% and averaged 5.5%, including 4.1% in the preoperatively asymptomatic patients. Realizing there are limits to this type of comparative analysis, patients with carotid disease undergoing CABG without CEA appear to have a higher risk of perioperative permanent stroke (5.5%) than those having combined CEA/CABG (3.1%). Two studies report the late outcome of asymptomatic patients who underwent CABG in the presence of uncorrected carotid disease without suffering a perioperative stroke, and are summarized in Table 8 [20, 37]. In these studies, with a combined total of 90 patients, 4 patients (4.4%) had strokes of which at least three (3.3%) were ipsilateral and 13% had TIAs over a follow-up period of 35 to 41 months. Although these particular populations were associated with only one stroke at the time of CABG [31], they serve as the only examples of the late stroke risk of unoperated carotid disease after CABG. As such, when this delayed stroke risk of 4.4% is combined with the perioperative stroke risk for the asymptomatic group of 4.9%, there would appear to be a cumulative stroke risk of 9% for the asymptomatic patients over a mean of 35 to 41 months.

In the present CEA/CABG study, there were no operative strokes and a 5% (2 of 40) late (mean, 46 months) stroke risk in the asymptomatic patients. In the other CEA/CABG studies noted above, which included patients with symptomatic carotid disease, the late (mean, 26 to 35 months) stroke risk was 4.8% and the late ipsilateral stroke risk was only 1.3%. The cumulative stroke risk for these CEA/CABG studies, including perioperative (3.1%) and late (4.8%) risk, would be estimated at 8% and includes many symptomatic patients. In addition, there were no late TIAs among the asymptomatic patients in our CEA/CABG group, as compared with a 13% late TIA rate in patients with carotid disease having only CABG. These late TIAs would imply the need for late CEA, with an associated operative risk. In the randomized study by Hertzer and associates [6], there was a stroke risk of 7.5% (4 of 53) associated with nonsynchronous CEA after CABG. By completing the CEA just before CABG, the

Table 8. CABG With Unoperated Major Carotid Disease: Late Events (>1 month)

Reference	Year	No. of Patients	Operation	Symptoms	Mean Follow-up (mo)	TIA (%)	CVA (%)	Ipsilateral CVA (%)
Barnes et al [20]	1985	40	CPB	Asymptomatic	35	15	2.5	
Schultz et al [37]	1988	50	CPB	Asymptomatic	41	11	6	6
Total		90			38	13	4.4	

CPB = cardiopulmonary bypass; CVA = cerebrovascular accident; TIA = transient ischemic attack.

operative stroke risk of CEA is incorporated into the CEA/CABG stroke risk, and the improved cerebral perfusion may help prevent perioperative stroke associated with hemodynamic instability. Also, one does not have the continued risk of embolic stroke or carotid occlusion occurring in the presence of known correctable carotid disease.

The late follow-up for our combined CEA/CABG series reveals an overall perioperative or late total stroke rate of 12% at 5 years and 14% at 8 years. Several other combined CEA/CABG series have reported 5-year stroke-free survivals of 91% to 98% [4, 6–9]. Freedom from late permanent ipsilateral stroke in our CEA/CABG series was 97% ± 2% at 8 years. Of the 6 patients with late strokes, 2 had known bilateral disease and suffered contralateral strokes that potentially could have been avoided by earlier contralateral carotid endarterectomy. Not all strokes are preceded by transient symptoms and not all symptoms are reported quickly enough to prevent stroke, which are good reasons to proceed with CEA at the time a diagnosis of severe carotid disease is made.

In summary, combined CEA/CABG is the preferred surgical approach to the vasculopath with severe combined carotid and coronary disease at the Brigham and Women's Hospital. These patients have a higher risk of stroke during CABG than patients without carotid disease, and this perioperative stroke risk may be reduced by the performance of CEA just before CABG. Combined CEA/CABG is an expeditious alternative in this high-risk population, avoids a subsequent hospitalization, anesthetic, and high-risk delay period, and provides long-term protection from ipsilateral stroke.

We thank the Cardiac Surgery Research Staff under the direction of Nancy Kinchla and Julie Lombara of Vascular Research for help with the data collection, Elizabeth Allred for statistical analysis, and Mary Ellen Schuster and Mary Ann Hartblay for preparation of the manuscript.

References

1. Bernhard VM, Johnson WD, Peterson JJ. Carotid artery stenosis: association with surgery for coronary artery disease. Arch Surg 1972;105:837–40.
2. Ennix CL, Lawrie GM, Morris GC, et al. Improved results of carotid endarterectomy in patients with symptomatic coronary disease: an analysis of 1,546 consecutive carotid operations. Stroke 1979;10:122–5.
3. Faggioli GL, Curl GR, Ricotta JJ. The role of carotid screening before coronary artery bypass. J Vasc Surg 1990;12:724–31.
4. Hertzer NR, Loop FD, Taylor PC, Beven EG. Combined myocardial revascularization and carotid endarterectomy. J Thorac Cardiovasc Surg 1983;85:577–89.
5. Brener BJ, Brief DK, Alpert J, Goldenkranz RJ, Parsonnet V. The risk of stroke in patients with asymptomatic carotid stenosis undergoing cardiac surgery: a follow up study. J Vasc Surg 1987;5:269–79.
6. Hertzer NR, Loop FD, Beven EG, O'Hara PJ, Krajewski LP. Surgical staging for simultaneous coronary and carotid disease: a study including prospective randomization. J Vasc Surg 1989;9:455–63.
7. Duchateau J, Nevelsteen A, Sergeant P, Flameng W, Suy R. Combined myocardial and cerebral revascularization. J Cardiovasc Surg 1989;30:715–22.
8. Pome G, Passini L, Colucci V, et al. Combined surgical approach to coexistent carotid and coronary artery disease. J Cardiovasc Surg 1991;32:757–93.
9. Vermeulen F, Hamerlijnck R, Defauw J, Ernst S. Synchronous operation for ischemic cardiac and cerebrovascular disease: early results and long-term follow-up. Ann Thorac Surg 1992;53:381–90.
10. Mehigan JT, Buch WS, Pipkin RD, Fogarty RJ. A planned approach to coexistent cerebrovascular disease in coronary artery bypass candidates. Arch Surg 1977;112:1403–9.
11. Emery RW, Cohn LH, Whittemore AD, Mannick JA, Couch NP, Collins JJ. Coexistent carotid and coronary artery disease. Arch Surg 1983;118:1035–8.
12. Rosner B. Fundamentals of biostatistics. 3rd ed. Boston: PWS-Kent Publishing, 1990.
13. Cox DR, Oakes D. Analysis of survival data. London: Chapman and Hall, 1984.
14. Hoffman RG, Blumlein SL, Anderson AJ, Barboriak JJ, Walker JA, Rimm AA. The probability of surviving coronary artery bypass surgery: five-year results from 1,718 patients. JAMA 1980;243:1341.
15. Amarenco P, Duyckaerts C, Christopher T, Henin D, Bousser MG, Hauw JJ. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. N Engl J Med 1992;326: 221–5.
16. Jones EL, Craver JM, Michalik RA, et al. Combined carotid and coronary operations: when are they necessary? J Thorac Cardiovasc Surg 1984;87:7–16.
17. Gardner TJ, Horneffer PJ, Manolio TA, et al. Stroke following coronary artery bypass grafting: a ten-year study. Ann Thorac Surg 1985;40:574–81.
18. Arom KV, Cohen DE, Strobl FT. Effect of intraoperative intervention on neurological outcome based on electroencephalographic monitoring during cardiopulmonary bypass. Ann Thorac Surg 1989;48:476–83.
19. Turnipseed WD, Berkoff HA, Belzer FO. Postoperative stroke in cardiac and peripheral vascular disease. Ann Surg 1980;192:365–8.
20. Barnes RW, Nix ML, Sansonetti D, Turley DG, Goldman MR. Late outcome of untreated asymptomatic carotid disease following cardiovascular operations. J Vasc Surg 1985;2: 843–9.
21. A Veterans Administration Cooperative Study. Role of carotid endarterectomy in asymptomatic carotid stenosis. Stroke 1986;17:534–9.
22. North American Symptomatic Carotid Endarterectomy Trial (NASCET). North American Symptomatic Carotid Endarterectomy Trial: methods, patient characteristics, and progress. Stroke 1991;22:711–20.
23. Cambria RP, Ivarsson BL, Akins CW, Moncure AC, Brewster DC, Abbott WM. Simultaneous carotid and coronary disease: safety of the combined approach. J Vasc Surg 1989;9:56–64.
24. Rice PL, Pifarre R, Sullivan HJ, Montoya A, Bakhos M. Experience with simultaneous myocardial revascularization and carotid endarterectomy. J Thorac Cardiovasc Surg 1980; 79:922–5.
25. Schwartz RL, Garrett JR, Karp RB, Kouchoukos NT. Simultaneous myocardial revascularization and carotid endarterectomy. Circulation 1982;66:97–101.
26. Babu SC, Shah PM, Singh BM, Semel L, Clauss RH, Reed GE. Coexisting carotid stenosis in patients undergoing cardiac surgery: indications and guidelines for simultaneous operations. Am J Surg 1985;150:207–11.
27. Reul GJ Jr, Cooley DA, Duncan JM, et al. The effect of coronary bypass on the outcome of peripheral vascular operations in 1093 patients. J Vasc Surg 1986;3:788–98.
28. Dunn EJ. Concomitant cerebral and myocardial revascularization. Surg Clin North Am 1986;66:385–95.
29. Perler BA, Burdick JF, Minken SL, Williams GM. Should we perform carotid endarterectomy synchronously with cardiac surgical procedures? J Vasc Surg 1988;8:402–9.
30. Minami K, Gawaz M, Ohlmeier H, Vyska K, Korfer R.

Management of concomitant occlusive disease for coronary and carotid arteries using cardiopulmonary bypass for both procedures. J Cardiovasc Surg 1989;30:723–8.

31. Barnes RW, Liebman PR, Marszalek PB, Kirk CL, Goldman MH. The natural history of asymptomatic carotid disease in patients undergoing cardiovascular surgery. Surgery 1981;90: 1075–83.
32. Breslau PJ, Fell G, Ivey TD, Bailey WW, Miller D, Strandness DE. Carotid arterial disease in patients undergoing coronary artery bypass operations. J Thorac Cardiovasc Surg 1981;82: 765–7.
33. Kartchner MM, McRae LP. Carotid occlusive disease as a risk factor in major cardiovascular surgery. Arch Surg 1982;117: 1086–8.
34. Ogren CO, Klamer TW, Towne JB, Bandyk DF. The role of noninvasive cerebrovascular testing in patients undergoing coronary artery surgery. Bruit 1983;7:22.
35. Ivey TD, Strandness DE, Williams DB, Langlois Y, Misbach GA, Kruse AP. Management of patients with carotid bruit undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg 1984;87:183–9.
36. Furlan AJ, Craciun AR. Risk of stroke during coronary artery bypass graft surgery in patients with internal carotid artery disease documented by angiography. Stroke 1985;16:797–9.
37. Schultz RD, Sterpetti AV, Feldhaus RJ. Early and late results in patients with carotid disease undergoing myocardial revascularization. Ann Thorac Surg 1988;45:603–9.
38. Johnsson P, Algotsson L, Ryding E, Stahl E, Messeter K. Cardiopulmonary perfusion and cerebral blood flow in bilateral carotid artery disease. Ann Thorac Surg 1991;51:579–84.

DISCUSSION

DR JOSEPH S. COSELLI (Houston, TX): It is an honor to be able to open the discussion on this report, and I would like to compliment Dr Rizzo on a very fine presentation. He and his associates are to be congratulated on what have to be rather spectacular results in the treatment of a very complex group of patients with combined carotid and coronary artery atherosclerosis as measured by an admirably low perioperative morbidity, including perioperative stroke and myocardial infarction as well as a low mortality rate. Having had the opportunity to review their manuscript in advance, for which I am grateful, I would, however, like to pose a couple of questions. I would like to first state that in the manuscript itself, there is a wealth of information evaluating a wide variety of subgroups not commonly addressed in the literature elsewhere.

Rizzo and associates compare patients with combined carotid and coronary disease to groups with isolated coronary artery disease undergoing CABG and isolated carotid disease undergoing isolated CEA. By their univariate analysis they were able to demonstrate that there is a clear and significant difference between these two groups, who are significantly different particularly as to characteristics including the incidence of hypertension, tobacco use, and the presence of left main coronary artery disease and diabetes. They do not have a group in which patients with concomitant carotid artery disease underwent isolated CABG and, therefore, very validly refer to the literature for comparison.

I would like to ask Rizzo and associates their justification in comparing the early and late results in these two clearly different groups. Second, if a comparison between two such groups, ie, concomitant versus isolated disease, is to be carried out, would not the comparison have benefited by a multivariate analysis to adjust statistically for the differences between the two groups and establish specific cohorts of patients in which a valid comparison analysis could be undertaken? Would it not have been better to carry out a comparison between patients with concomitant disease undergoing simultaneous treatment of carotid and coronary disease versus the nonsimultaneous or staged or selected treatment of the various disorders?

In their review of the literature Rizzo and associates aptly point out an article by Norm Hertzer in which a comparison of such description was undertaken in a prospective, randomized evaluation in a highly selective group of patients with unilateral asymptomatic carotid lesions requiring CABG in whom either a combined operation or CABG followed by a delayed CEA was undertaken. This staged operation had a 14% stroke risk versus a combined operation stroke risk of only 2.8%. If indeed, as Rizzo and associates suggest, and I think most of us would concur, a controversy still exists regarding the optimal treatment and surgical management of patients with multisystem atherosclerosis, should not a multicenter, prospective, randomized trial be undertaken to accrue enough patients for a satisfactory statistical analysis, adjusting for the anatomic diversity and clinical characterizations to better establish the preferred treatment in specific cohorts of patients?

Regardless, I concur completely with their conclusions, and they have presented a very fine group of patients and a spectacular analysis. I would like to thank The Society for the opportunity to open the discussion on this very important and extremely fine report.

DR RIZZO: Thank you, Dr Coselli, for your review. Our study was initially designed to simply examine our results with combined CEA/CABG. We then realized that to really understand the problem we needed to know what happened both with patients who underwent isolated operations for isolated carotid or coronary disease, as well as with patients who underwent isolated CABG with combined disease. We had experience with patients having isolated operation for isolated disease, but not in those having isolated CABG in the presence of known carotid disease, because our policy has been to perform combined CEA/CABG in that group. Because we did not have our own patients to study with combined disease having isolated CABG, we were forced to go to the literature to define the results for this approach. Some studies have shown as high as a 14% risk of perioperative stroke in patients who have severe carotid disease undergoing isolated CABG. This stroke risk seems too high to accept, and I think some patients may be suffering strokes that could otherwise be prevented.

The other point that we tried to bring out in our report was that in addressing major carotid disease at the time it is diagnosed, you do not have to then anxiously follow up patients after coronary operations and watch them have a stroke in the presence of known major carotid disease. In some of these other studies that provided late follow-up in patients who underwent CABG without carotid endarterectomy, there was as high as a 13% risk of TIA in late follow-up. Those patients would obviously then come to CEA, which would entail an inherent risk of stroke.

Combined carotid and coronary disease can be managed in multiple ways, and a multicenter trial would be helpful. Our approach has been to combine CEA with CABG, and those are the only data that we have on patients with known carotid disease.

DR STEVEN R. GUNDRY (Loma Linda, CA): I also would like to compliment Rizzo and associates on an extremely important report in an area of considerable controversy. We, like them, believe, and it is a belief rather than proven fact, that people with severe carotid and coronary artery disease are best approached in a single operative setting. One of our medical students, Clifford Eke, has recently reviewed our experience in a later time period, beginning in 1986, and will soon be reporting his results on 42 patients who have had this combined approach in groups very similar to those reported here. We, however, had no perioperative strokes and only one transient neurologic event on the contralateral side. We also found a considerable difference in the length of operation when two surgical teams were used as opposed to a single surgical team. With thoracic surgeons doing both parts of the operation, the time in the operating room was considerably shortened as opposed to when a vascular surgeon did the carotid portion and a thoracic surgeon did the coronary portion. We found the median stay in the hospital was 8 days.

I have two questions. First of all, did you compare hospital days for this combined approach versus CABG or CEA alone to justify this combination of techniques? Second, did you find any difference in results either in strokes or in time in the operating room if two surgical teams were used rather than a single surgical team?

Again, I compliment the authors on bringing this very important information to our attention.

DR RIZZO: All of our procedures were done using two teams; that has been the policy at our hospital. So I cannot provide any comparative data there. It is commendable to have no strokes, but you have a small series. I think that the longer and the larger the series and the sicker the patients, the more strokes one can expect to have. There is certainly room for improvement, and I think there are a couple of areas where we might be able to increase the freedom from stroke at operation. These would include screening patients more thoroughly, monitoring the electroencephalogram at the time of CABG in patients in whom there is known cerebrovascular disease, increasing perfusion pressure in these patients based on electroencephalographic changes, and increasing carbon dioxide tension, which can increase cerebral blood flow, and I think another area that is growing in popularity is echography of the aorta. I think the ascending aorta and arch are often responsible for these strokes after coronary operations, even in this group with combined disease. If we can identify those patients who have ulcerated plaques in the ascending aorta and arch, we might be able to alter our techniques to decrease the risk of embolic stroke.

DR EDWARD A. PASCOE (Winnipeg, Manitoba, Canada): There was an article in *The Annals of Thoracic Surgery* in the mid-1980s recommending a slightly different approach in which the carotid artery is exposed, then the patient is cannulated and placed on hypothermic cardiopulmonary bypass. The carotid endarterectomy is performed with the additional potential protection of cerebral hypothermia, then carrying on with the cardiac procedure and closing both incisions at the end. We have used that technique in Winnipeg a handful of times with very gratifying results. Have you considered that approach, sir?

DR RIZZO: We have considered that approach; we have not used it. I think it is an excellent option.

Vascular Anatomy of the Gastric Tube Used for Esophageal Reconstruction

Dorothea M. I. Liebermann-Meffert, MD, Renate Meier, MD, and
J. Rüdiger Siewert, MD

Departments of Surgery, Klinikum rechts der Isar, Technische Universität, München, Germany, and University Hospital, Kantonsspital, Basel, Switzerland

This study investigates the actual, as contrasted with the presumed, blood supply of the greater curvature gastric tube commonly used to reconstruct the gullet after esophagogastrectomy. Arterial and venous corrosion casts of this tube were created in 30 cadavers and demonstrated the following: (1) The right gastroepiploic artery is the exclusive conduit of blood in the pedicle. (2) The contribution of the right gastric artery is negligible. (3) Although tributaries of the left gastroepiploic artery are distributed over the central portion of the tube, the connection between the right and left gastroepiploic vessels is minute. (4) The blood supply of the cranial 20% of the greater curvature tube is through a microscopic network of capillaries and arterioles. These findings constitute an anatomical argument for extremely gentle handling of the stomach throughout its mobilization, during construction and positioning of the tube, and during the anastomosis.

(Ann Thorac Surg 1992;54:1110–5)

When it comes to operations for cancer of the esophagus or esophagogastric junction, proponents of total thoracic esophagectomy with a cervical anastomosis are both numerous and persuasive [1–6]. Arguments for creating a greater curvature gastric tube and positioning the esophagogastrostomy in the neck rather than in the chest include better surgical results, improved functional results, and a reduction in the incidence of fatal mediastinitis in the event of anastomotic dehiscence. Nevertheless, nonlethal leaks still occur and are apt to be followed by stenosis and dysphagia [3–5]. A less than optimal blood supply is often blamed, but it is unclear whether the likely factors are arterial or venous, technical or anatomical.

According to current concepts [1–8], the gastric tube receives its circulation entirely from its caudal end, namely, the right gastroepiploic and right gastric arteries. Venous drainage follows the same lines. Iatrogenic squeezing, bruising, or kinking of these vessels or their tributaries can set the stage for ischemia and anastomotic dehiscence. Other factors relating to the adequacy of the blood supply may include (1) sacrifice of the left gastric and short gastric arteries, (2) variations in the distribution of the supplying vessels, (3) poor venous drainage, (4) arteriosclerosis of the gastroepiploic artery, (5) ischemia caused by stretching of a short tube, and (6) construction of a needlessly narrow tube. The purpose of this study was to examine whether a nonreversed gastric tube makes anatomical sense.

Material and Methods

Thirty human autopsy specimens, 19 male and 11 female, aged 38 to 80 years (median age, 70 years) were the subject of this study. Any specimen with previous abdominal or vascular disease [6] was excluded.

Injection Material

The cold-setting synthetic resin Beracryl (Monomer/Polymer Acryl-Industrie Kunststoff; Troller AG, Fulenbach, Switzerland) was used. The arterial system was demonstrated in 18 casts and the venous system in 12, similar to our previous report [6]. We chose a polymer with a particle size of 120 μm and used red for arteries and blue for veins. This resin displayed the macroscopic vascular architecture down to the size of arterioles in a permanent, multidimensional corrosion cast.

Technique

Nine to 24 hours after death, the abdominal organs and vessels were removed en bloc from the retroperitoneum. The stomach was irrigated with Ringer's solution to slow down the autolytic process. The thoracic aorta and vessels to the kidneys and liver were ligated; the other vessels were irrigated as previously described [6].

A generous Kocher maneuver was carried out to elevate the pylorus to the level of the esophageal hiatus. Thorough ligation of vascular connections was mandatory during this step because leakage from even small vessels spoiled the cast. The vessels of the greater omentum were divided between ligatures exterior to the gastroepiploic arcade. After ligation of the short gastric vessels, a tube 4 to 5 cm wide was constructed from the greater gastric curvature. An Auto Suture multifire GT stapler (United States Surgical Corporation, Norwalk, CT) was used with

---

Accepted for publication March 12, 1992.

Address reprint requests to Prof Dr Liebermann-Meffert, Department of Surgery, Klinikum rechts der Isar, Technische Universität, Ismaninger Str. 22, D-8000 München 80, Germany.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

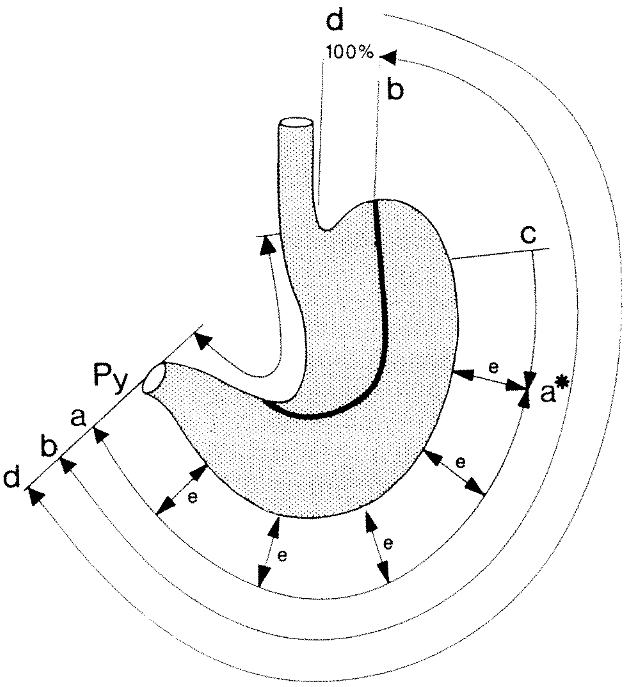


Fig 1. Measurements: lengths of right gastroepiploic vessel (Py–a) and left gastroepiploic vessel (a*–c); distance from pylorus to tip of fundus (Py–b); distance from pylorus to cardiac angle (Py–d); and distance from gastroepiploic vessel to greater curvature (e).*

the loading units TA 55-p (L 0757) and TA 90-p. The staple line was not reinforced by sutures.

The gastric tube was stabilized using water-filled condoms placed into its lumen. The resin was injected through catheters in the aorta or portal vein. Injection pressure was applied by hand and was identical in all specimens. Flow of the resin was controlled under direct vision. Further procedures were similar to those described previously [6]. Only casts of good quality were included.

Documentation

Different lengths were measured in the fresh and injected specimens at various steps in the procedure (Fig 1). The vascular casts were outlined (Fig 2) and documented as previously described [6]. Length, width, and distribution of the vessels were taken from the drawings, and the ratio of the length of each gastroepiploic vessel to the total length of the greater gastric curvature, as well as to that of the gastric tube, was determined. The relatively large particle size of Beracryl displayed the macrovasculature of the tube but not the microvascular submucosal and mucosal network. This resulted in an apparent disparity in the length of the anatomical tube and the vascular corrosion cast. This difference is called the "missing length" (Fig 3).

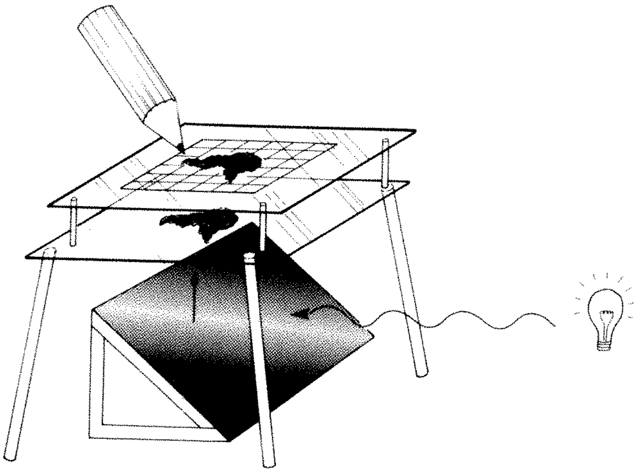


Fig 2. Method of reproduction of the vascular tree. The cast is placed between two glass sheets and illuminated from below using a mirror. The silhouette is transferred 1:1 to graph paper on the upper glass sheet and later schematized.

Results

Esophageal and Gastric Dimensions

The length of the esophagus between the cricoid cartilage and the cardiac notch ranged from 22 to 34 cm (average length, 27 cm) depending on the height of the body (153 to 187 cm). The mean length was 24 ± 2 cm (± the standard deviation) in female and 28 ± 3 cm in male specimens.

The greater gastric curvature between the pylorus and the tip of the gastric fundus (see Fig 1) was 38 ± 4 cm long without any difference between sexes (Table 1). The meandering gastroepiploic arcade (see Fig 1) was 47 ± 8 cm long and the lesser curvature, 17 ± 3 cm long. The gastric tube ranged from 28 to 42 cm in length (mean

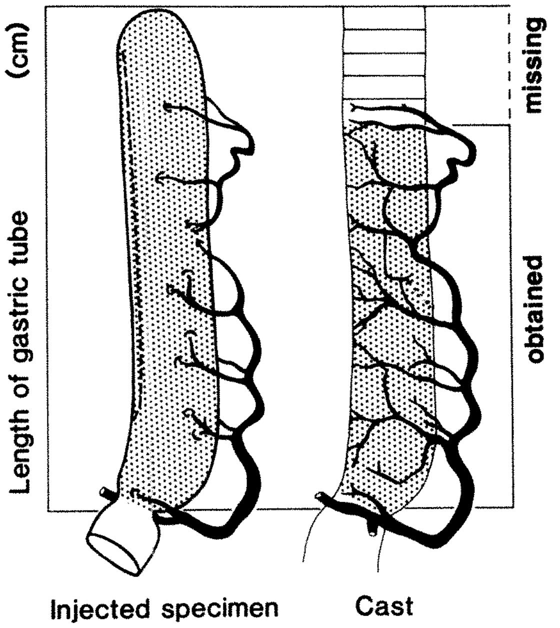


Fig 3. Macroscopic aspect of the gastric tube with exterior vessels displayed on the injected uncorroded specimen and the corroded cast. The distance between the pylorus and the tip of the gastric tube was measured. After corrosion, the upper segment of the tube was missing.

Table 1. Evaluation of Vascular Anatomy[a]

No. of Specimens	Display	Distance[b] Pylorus to Fundus (Py–b)	Distance[b] Pylorus to Anastomosis (Py–a)	Ratio (%) (a:b)	Distance to Tip of Tube[b]	% Missing (Py–b)
Arteries						
16	Angiogram of stomach	38 ± 7	21 ± 4	56	. . .	. . .
18	Cast of stomach	39 ± 7	25 ± 4	60	. . .	. . .
18	Cast of tube	37 ± 4	19 ± 3	63	30 ± 5	20
Veins						
11	Cast of stomach	39 ± 7	22 ± 5	58	. . .	. . .
12	Cast of tube	36 ± 5	18 ± 2	65	31 ± 5	23
75	Specimens	38	21	60	31	22

[a] Dimensions correspond to measurements in Figure 1. Values from the whole stomach were obtained with similar technique from resin vascular corrosion casts and angiograms after in situ arterial injection of barium-gelatin. They are listed here for comparison. Length of the greater gastric curvature as the distance from the pylorus to the tip of the gastric fundus (Py–b) or the tip of the gastric tube is shown. The distance from the pylorus to the anastomosis between the right and left gastroepiploic vessels (Py–a) and the distance to the tip of the gastric tube in the cast are shown. The ratio (a:b) is the relative distance from the pylorus to the anastomosis calculated as a percentage. [b] Data are shown as the mean ± the standard deviation in centimeters.

length, 39 ± 3 cm) and was 4 cm in width. Further details are provided in Table 1.

Arterial and Venous Vascular Distribution in the Gastric Tube

The cast contained the complete arterial or venous vascular tree of the gastric tube for vessels with diameters larger than 120 μm. The right gastroepiploic artery was the exclusive source of blood to the gastric tube (Figs 4, 5). Injection of the resin into the aorta showed that the right gastroepiploic artery received its blood from the celiac axis through the gastroduodenal artery and, to the same extent, from the superior mesenteric artery. When the superior mesenteric artery alone was injected after ligation of all other vessels, complete filling was obtained through the pancreatic arcades (see Fig 5). The remnants of the left gastroepiploic artery (see Fig 5) and vein (Fig 6) were well displayed in all the casts. This artery, which originated from the splenic artery, was located in the bulgy portion of the greater omentum caudal to the spleen. A fine anastomosis connected the left and right gastroepiploic vessels, either extramurally or within the wall of the former greater gastric curvature (see Fig 6). The anastomosis was located 19 ± 3 cm from the pylorus (see Table 1), a distance representing 60% of the length of the greater gastric curvature (Fig 7). The right gastric artery was short (see Fig 4) and its diameter, minute (<200 mm). When the left gastroepiploic artery was severed from its origin, the resin penetrated by way of the right gastroepiploic artery through the anastomosis (see Figs 5, 6) into the remnant of the left gastroepiploic artery. Inflow was clearly reversed compared with the normal direction of flow in the left gastroepiploic vessel. Reversed flow was even more distinct in the wall of the former fundus, where the inflow through the short gastric arteries was completely cut off.

Compared with the arterial casts, the venous casts had a superior display (see Fig 6) because the internal diameters of the veins were larger than those of the arteries, and the replicas were therefore more impressive. No essential variations in the distribution or proportion of the vessels, however, were found compared with the arterial pattern (see Table 1).

When the length of the gastric tube before injection was defined as 100% (see Fig 1), approximately 20% of the upper part of the tube in both the arterial and venous casts was not displayed (see Table 1; Figs 3, 7). This occurred because the resin had not penetrated the microvascular plexus.

Comment

When the stomach is used to replace the esophagus, the anastomosis with the cervical stump tends to be made at the fundus [7]. More recently, an isoperistaltic tube, 4 to 6 cm wide, constructed from the greater gastric curvature has been preferred [1–5, 8, 9]. It was found that the right gastroepiploic pedicle provides adequate nutrition to the tube, and the short gastric vessels could be ligated without obvious wall damage. Nevertheless, postoperative complications such as anastomotic dehiscence and leaks [2, 3, 5] suggest the potential for some circulatory problems. Intestinal fistulas in the neck, although less dangerous than elsewhere, cause morbidity and prolong hospitalization.

The idea of the isoperistaltic tube was based on the pattern of vessels obtained from arteriograms of the whole stomach [1, 7, 10–12] and not on study of the tube itself. The claim that the tip of the former gastric fundus after its anastomosis to the stump of the cervical esophagus is less vascularized [7] required substantiation. If it is true that vascularization of the fundus is inadequate, partial fundus resection would make sense, even if there is loss of tubal length. For ethical and technical reasons, we were unable to study this problem in patients with replaced esophagi and instead used gastric tubes constructed in human corpses. For the multidimensional display of the vessels, we took advantage of a commer-

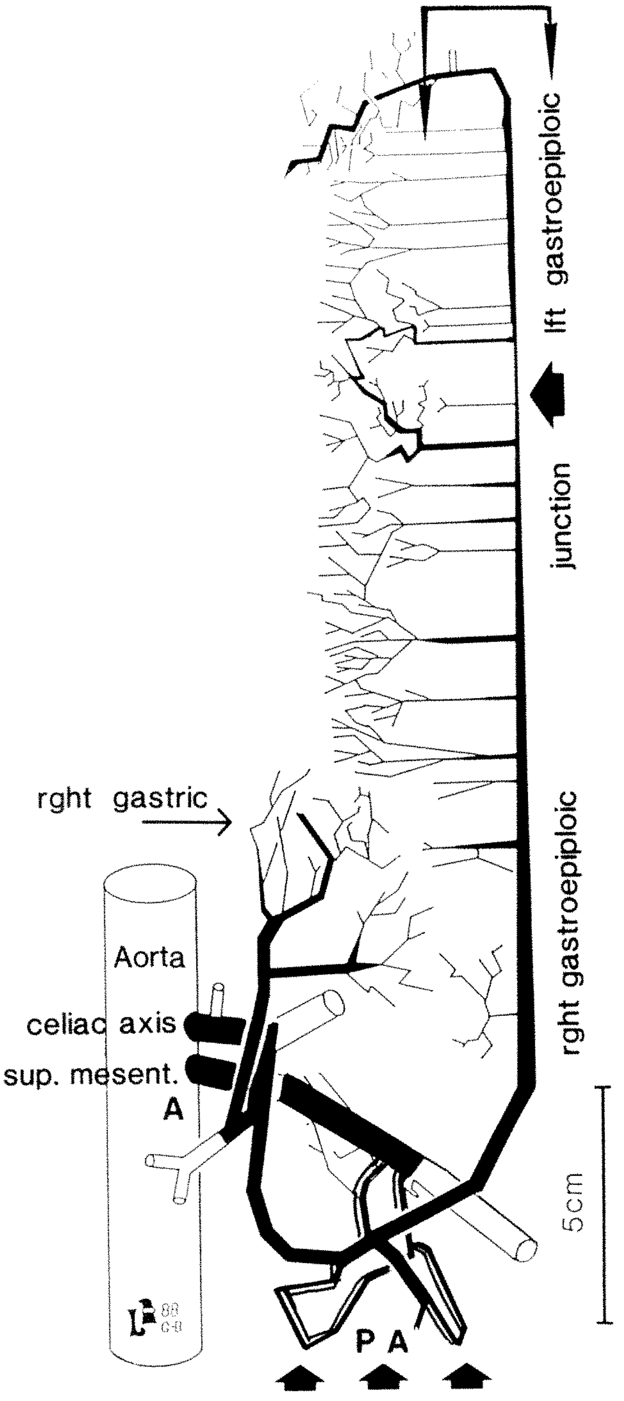


Fig 4. Common pattern of arteries supplying the gastric tube. Celiac axis and superior mesenteric artery (sup. mesent. A) *are sources of the right* (rght) *gastroepiploic artery. The gastric branches of the gastroepiploic arcade are shown by the U-shaped double arrow* (▼▼) *and the pancreatic arches* (PA) *by three fat arrows* (▲▲▲). *The single arrow* (◀) *indicates the location of the gastroepiploic anastomosis.* (lft *= left.*)

cially available synthetic resin that we adjusted to a particle size of 120 μm to exclude microvascular penetration. A too high density of the vascular cast by numerous small vessels would have confused the view. The color in the resin allowed control of injection flow by direct vision.

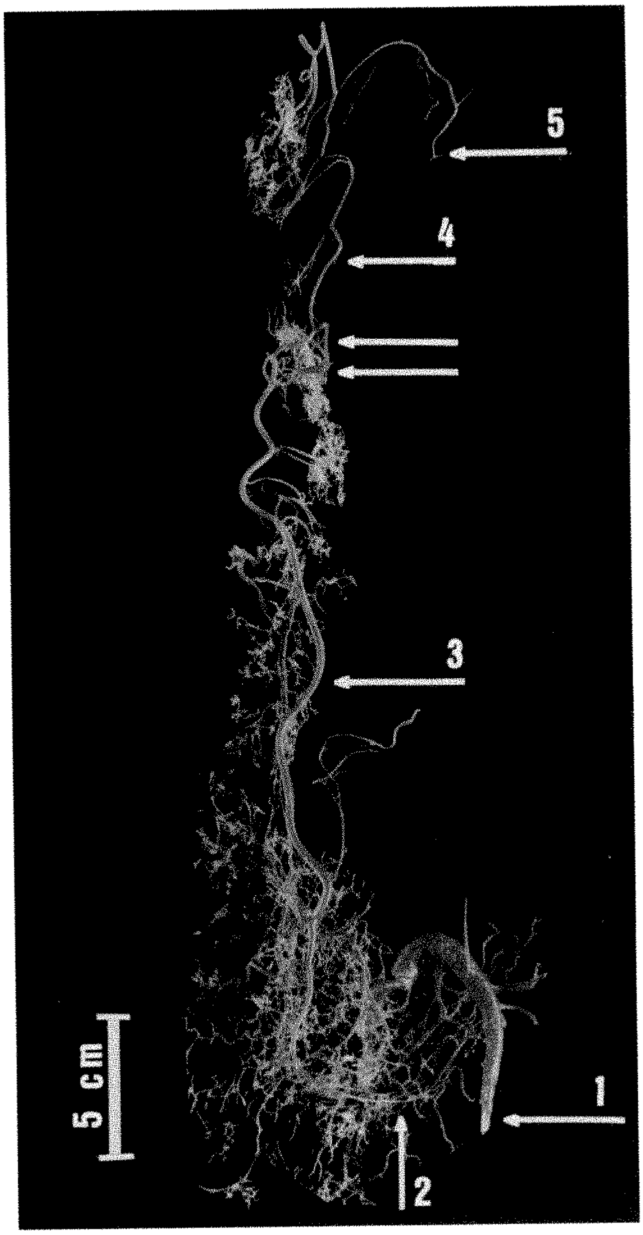


Fig 5. Arterial vascular cast of the gastric tube after resin injection through the superior mesenteric artery (1). This filled the pancreatic arcades (2), the right gastroepiploic artery (3), the remnant of the left gastroepiploic artery (4), their anastomosis (double arrows), *and the epiploic artery (5) completely.*

Our results confirmed that the nutrition of the gastric tube depends entirely on the right gastroepiploic artery. When considered in terms of the length of the greater gastric curvature as measured from the pylorus, it became obvious that 60% of the tube was directly supplied by that vessel and its branches and another 20% toward the cranial end, through its minute connection to the left gastroepiploic vessel. The various branches, circumferentially arranged and interconnected, provided ample vascularization to the wall of the tube. A fact not previously appreciated is that the right gastroepiploic artery receives equal-sized branches from both the celiac axis and the superior mesenteric artery.

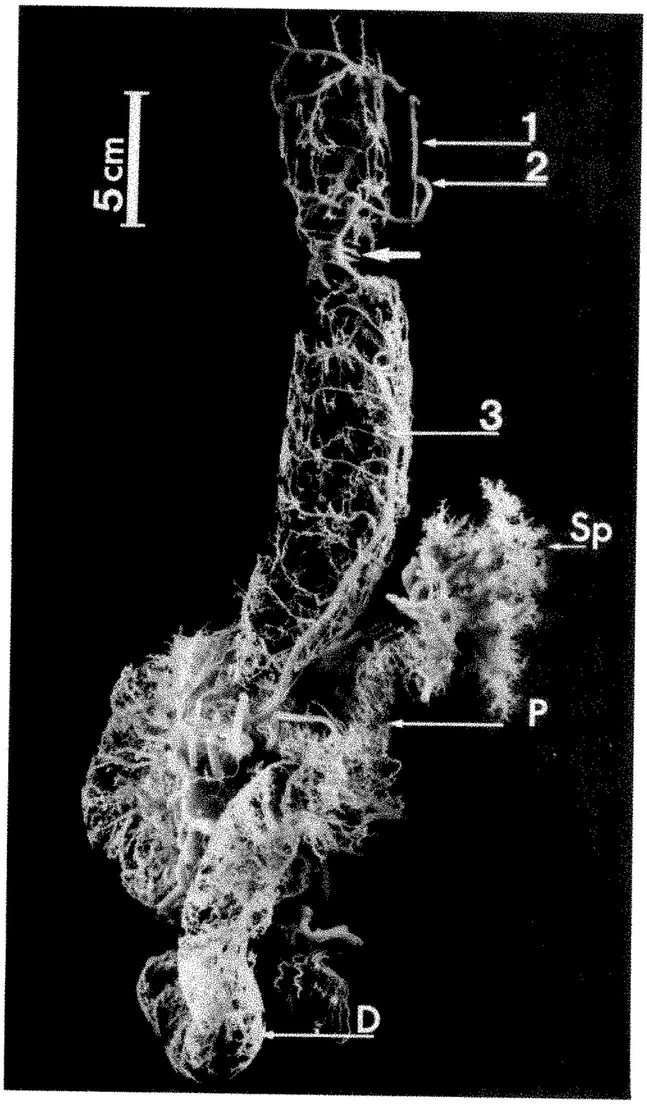


Fig 6. Venous vascular cast of the gastric tube obtained after resin injection through the portal vein. The left gastroepiploic vein (1), the epiploic vein (2), and the supplying area are well displayed forming an intramural connection (arrow) *to the right gastroepiploic vein (3). The tip of the tube is not shown because the minute vascular diameter did not allow transit of the resin. Dimensions and pattern were similar to those of the arteries.* (D = *duodenum;* P = *pancreas;* Sp = *spleen.)*

The importance of the right gastric artery to the blood supply of the tube has been stressed [7, 9]. However, tension at the anastomotic line in the neck is less and the gastric pull-up easier with division of the right gastric artery. In our specimens, this small vessel was of little importance, and there is no anatomical reason to preserve it. Tension on the anastomosis remains a problem during healing, and most of the time is caused by a short gastric tube. Our work and that of others [1, 8, 9, 13] show that the greater gastric curvature is longer than the esophagus. Therefore, mobilization of the stomach, an extensive Kocher maneuver, and proper construction of the tube per se should nearly always afford ample length for a tension-free anastomosis.

As far as the width of the tube is concerned, the ideal line of section from the stomach seems to be the anastomotic site between the various small branches of the left gastric and right gastroepiploic vessels in both the anterior and posterior walls. This line is 4 to 5 cm from the greater gastric curvature, a finding that supports the clinical practice to use the gastric tube rather than the whole stomach.

Obstruction by arteriosclerotic lesions may eventually compromise the vascular supply of the gastric tube [12]. We did not study this problem in detail because severe arteriosclerosis, confirmed in angiograms, is a contraindication for esophagectomy with gastric tube replacement. In addition, autopsy specimens showing any vascular disease had very poor filling results [6] and were excluded. Palpation of the gastroepiploic arcade itself during selection of the specimens did not reveal any arteriosclerotic changes in our material. This observation agrees with the histological studies of Suma and Takanashi [14], who found almost no involvement of the gastroepiploic arteries even in patients with major occlusive vascular disease at other sites and who used the gastroepiploic vessels as a conduit for coronary artery bypass grafting.

The wide distribution of the resin within the complete arterial and venous architecture of the lower portion of the tube established that the "missing vascular tree" from the upper 20% of the uncorroded tube was related to the small diameter of the local and regional vessels. Injection with Mercox, which is a resin of far smaller particle size, showed a dense microvascular network in the mucosa and submucosa but no larger vessels [15, 16]. This rich intramural vascularity with the evident continuity of vessels is the reason why the upper portion of the mobilized gastric tube retains a sufficient blood circulation and why the surgical esophagogastric anastomosis most of the time is not greatly compromised by ligation of the short gastric vessels.

The natural vascular supply to the cranial part of the tube is further distorted by the inevitable separation of the left gastroepiploic artery from its splenic source. The remnant of the left gastroepiploic artery fills easily through the right gastroepiploic vessels. However, the inflow to the cranial part of the tube is reversed, and in the living, reversed flow may signify impaired flow. Based on the anatomical findings, shortening the upper portion of the gastric tube seems to be an important step to improve the vascular situation at the site of anastomosis.

Our casts have shown a consistent pattern of an excellent vascular distribution in the wall of the gastric tube, which implies adequate circulation. The studies, however, were performed in human corpses. The injection conditions were optimal without any resistance to resin flow in the vessels. One therefore may argue the validity of our findings in respect to the blood supply in the gastric tube at the time of construction of the tube. Operative manipulation may provoke vascular spasm, and the circulation may be worse than expected from the anatomical conditions. Pulling up the gastric tube through the narrow aperture of the upper chest may mechanically impair

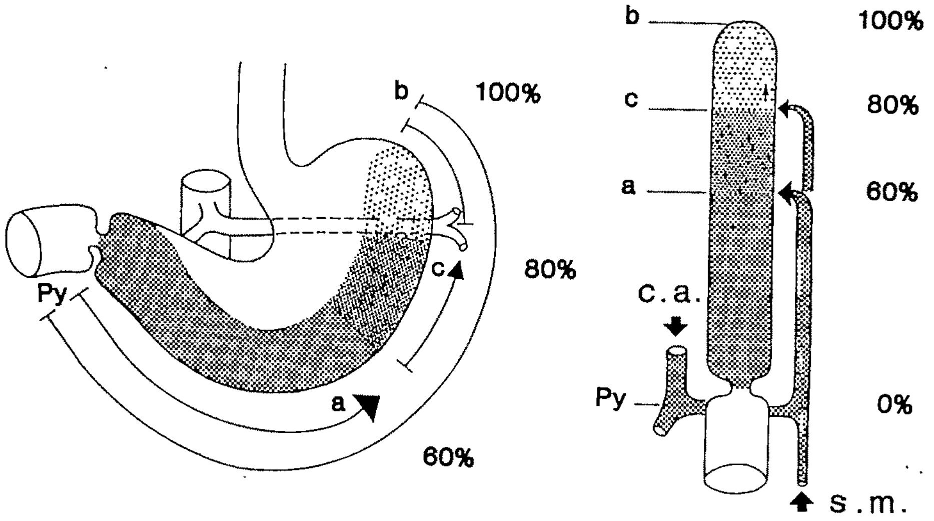


Fig 7. Anatomical features of blood supply to the wall of the gastric tube. As reasonably thick vessels (artery, 3- to 4.2-mm internal diameter; vein, 3.2- to 5.1-mm internal diameter), the right gastroepiploic vessels (Py–a) amply supply the lower 60% of the tube. The next 20% is supplied through the remnant of the left gastroepiploic artery (a–c), and the most cranial 20% (c–b) is supplied only through the submucosal and mucosal microvascular network. Distances shown are from the pylorus to the gastroepiploic anastomosis (Py–a), from the pylorus to the tip of the fundus or tube (Py–b), and from the pylorus to the end of the gastroepiploic vessels (Py–c). Routes through the celiac axis (c.a.) *and the mesenteric vessels* (s.m.) *are indicated by* arrows.

the circulation. Tension may be the consequence of either a tube that is too short (inadequately mobilized) or a tube that has too long a route, eg, through the anterior mediastinum. Furthermore, when reconstruction is performed in the anterior mediastinum, the upper chest aperture is even narrower and the circulation of the upper end of the gastric tube might be worsened. This situation cannot be simulated in our experimental design. The presence of extremely fine nutritional vessels in conjunction with reversed flow might explain the failure of the anastomosis to heal if the fine vessels are ruined by tension, rough handling, or compression at the thoracic inlet.

In conclusion, two points deserve emphasis. First, when the anastomosis of the gastric tube is made to the cervical esophagus one can count on an optimal circulation for two thirds the total length of the gastric tube. Second, the dense vascular network within the gastric tube can compensate for severance of the short gastric and left gastric arteries. Manipulation, tension, and strangulation of the upper portion of the tube may compromise the intramural network and jeopardize the esophagogastric anastomosis. When the vascularity of the stomach side of the anastomosis is doubtful, resecting the upper 6 to 8 cm of the gastric tube makes anatomical sense.

Funded in part by the International Foundation for Postgraduate Surgery, Basel, Switzerland.

The generous cooperation of Prof M. Mihatsch, Department of Pathology, Kantonsspital, Basel, for provision of autopsy specimens and laboratory facilities is greatly appreciated. We are grateful to Prof C. Hiebert, Toronto, Ontario, Canada, for editorial help. The technical support of Mrs S. Vosmeer and of Mr D. Hund and Mr H. Hartmann, Photoabteilung, Kantonsspital, Basel, is gratefully acknowledged. Thanks also are due to Mrs K. Luxenburger, München, for secretarial assistance.

References

1. Akiyama H, Miyazono H, Tsurumaru M, Hashimoto C, Kawamura T. Use of the stomach as an esophageal substitute. Ann Surg 1978;188:606–10.
2. Devitt PG, Jamieson GG. Hand-sewn anastomoses of the esophagus. In: Jamieson GG, ed. Surgery of the esophagus. Edinburgh: Churchill Livingstone, 1988:703–12.
3. Peracchia A, Bardini R, Asolati M, Scibetta D. Esophagovisceral anastomotic leak: a prospective statistical study of predisposing factors. Thorac Cardiovasc Surg 1988;95:685–91.
4. Siewert JR, Bartels H, Lange J, Roder JD, Hölscher AH. En bloc esophagectomy—when to reconstruct the food passage? In: Ferguson MK, Little AG, Skinner DB, eds. Diseases of the esophagus, vol I: Malignant diseases. Mt. Kisco, NY: Futura, 1990:253–60.
5. Skinner DB. Curative surgery for esophageal carcinoma. In: Jamieson GG, ed. Surgery of the esophagus. Edinburgh: Churchill Livingstone, 1988;617–22.
6. Liebermann-Meffert D, Lüscher U, Neff U, Rüedi TP, Allgöwer M: Esophagectomy without thoracotomy: is there a risk of intramediastinal bleeding? Ann Surg 1987;206:184–92.
7. Stelzner F, Kunath U. Ergebnisse bei oesophagointestinalen Anastomosen und Untersuchungen der Durchblutung des dafür mobilisierten Magens. Chirurg 1977;48:651–6.
8. Collard JM, Otte JB, Jamart J, Reynaert M, Kestens PJ. An original technique for lengthening the stomach as an oesophageal substitute after oesophagectomy. Preliminary results. Dis Esophagus 1989;2:171–4.
9. Yamato T, Hamanaka Y, Hirata S, Sakai K. Esophagoplasty with an autogenous tubed gastric flap. Am J Surg 1979;137:597–602.
10. Usadel W. Untersuchungen über die Gefässversorgung des Magens zum Zweck seiner plastischen Verwendbarkeit. Langenbecks Arch Klin Chir 1925;138:401–27.
11. Levasseur JC, Couinaud C. Etude de la distribution des artères gastriques. Incidences chirurgicales (1 et 2). J Chir (Paris) 1968;95:57–78,161–76.
12. Thomas DM, Langford RM, Russell RCG, Le Quesne LP. The anatomical basis for gastric mobilization in total oesophagectomy. Br J Surg 1979;66:230–3.
13. Goldsmith M, Akiyama H. A comparative study of Japanese and American gastric dimensions. Ann Surg 1979;190:690–3.
14. Suma H, Takanashi R. Arteriosclerosis of the gastroepiploic and internal thoracic arteries. Ann Thorac Surg 1990;50:413–6.
15. Gannon B, Browning J, O'Brien P, Rogers P. Mucosal microvascular architecture of the fundus and body of human stomach. Gastroenterology 1984;86:866–75.
16. Raschke M, Lierse W, van Ackeren H. Microvascular architecture of the mucosa of the gastric corpus in man. Acta Anat (Basel) 1987;130:185–90.

Absent Pulmonary Valve Syndrome: Operation in Infants With Airway Obstruction

Kevin G. Watterson, FRACS, Torsten K. Malm, MD, PhD, Tom R. Karl, MD,
and Roger B. B. Mee, FRACS

Royal Children's Hospital, Melbourne, Victoria, Australia

From 1979 through 1991, 19 infants with absent pulmonary valve syndrome and airway obstruction were seen for surgical treatment. All patients underwent extensive pulmonary artery aneurysmorrhaphy using cardiopulmonary bypass. Fourteen patients had simultaneous transatrial ventricular septal defect (VSD) closure, infundibular resection, and placement of a short transannular patch; 2 had transventricular VSD closure and infundibular resection without a transannular patch; 1 underwent transventricular VSD closure and transannular patching; and 2 underwent pulmonary artery aneurysmorrhaphy alone with the VSD left open. All 19 infants had good hemodynamics when taken from the operating theater, but 3 died postoperatively of severe airway obstruction, despite further tracheobronchopexy procedures in 2 (hospital mortality rate, 16%; confidence limits, 7% to 29%). Among the 16 patients discharged from the hospital, there was one late death. Five other patients have required reoperation for branch pulmonary artery stenosis (n = 2), residual airway obstruction resulting from persistent pulmonary artery dilatation (n = 1), closure of VSD (n = 1), and homograft valve insertion for pulmonary incompetence and right ventricular dysfunction (n = 1). There are 15 long-term survivors. Eight of them have episodic bronchospasm of mild to moderate severity, and all are responsive to sympathomimetic bronchodilator aerosols. The remaining 7 are asymptomatic.

(Ann Thorac Surg 1992;54:1116–9)

Absent pulmonary valve syndrome is a rare congenital cardiac lesion, the components of which include dysplasia and severe incompetence of the pulmonary valve, annular stenosis (usually not severe), and dilatation of the pulmonary artery (PA) system leading to tracheobronchial compression of varying degree [1, 2]. Presentation is often in infancy, with severe progressive airway obstruction. Management of this form of the condition has proved difficult because of an inability to consistently obtain relief of airway obstruction. Consequently, patient survival has been poor, and debate has continued regarding the most appropriate form of surgical management [3, 4]. Medical management with long-term ventilation has had a very high mortality [5, 6]. Recently reported series have focused on the role of pulmonary incompetence in this condition, and it has been suggested that optimum results are obtained when a pulmonary valve is inserted [7, 8]. This prompted a review of our surgical strategy, which emphasizes the technique of pulmonary aneurysmorrhaphy rather than valve insertion [9].

Material and Methods

Patient Population

During the period 1979 through 1991, 19 infants, 9 female and 10 male, were seen with absent pulmonary valve syndrome and airway obstruction (8 were ventilator dependent). Older children without airway obstruction were not included in this series. Mean age and weight at operation were 5.2 months (range, 4 days to 14 months) and 5.1 kg (range, 1.7 to 10.2 kg), respectively.

All 19 patients had a ventricular septal defect (VSD). Additional associated congenital cardiac abnormalities occurred in 4 patients: double aortic arch (n = 1), anomalous left PA arising from the aorta (n = 1), right lower lobe sequestration (n = 1), and a left superior vena cava draining to the coronary sinus (n = 1). In 15 patients, the diagnosis was made using a combination of echocardiography and cardiac catheterization, whereas echocardiography alone was used in the remaining 4 patients. Preoperative PA pressures were measured in 10 patients, and mean PA pressure ranged from 9 to 35 mm Hg (mean pressure, 19 mm Hg). Preoperative cinetracheobronchograms were obtained in 17 of the 19 patients. All showed anteroposterior compression of the lower trachea and right and left main bronchi, best seen in the lateral view.

Operative Technique

All patients underwent attempted relief of airway obstruction, mainly by extensive PA aneurysmorrhaphy. Pulmonary artery banding was not employed. In the earlier phase of the series, profound hypothermia and circulatory arrest using a single venous cannula was used. More recently, cardiopulmonary bypass with moderate hypothermia and two venous cannulas has been employed in 8 patients weighing more than 3 kg.

Accepted for publication March 20, 1992.

Address reprint requests to Dr Karl, Victorian Paediatric Cardiac Surgical Unit, Royal Children's Hospital, Flemington Rd, Parkville, Victoria, 3052, Australia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Summary of Patient Data

Patient No.	Age (mo)	Year of Operation	Type of Operation[a]	Reoperation (interval)	Status
1	7	1979	2	6 mo	Died (at reop)
2	5	1980	2	No reop	Well
3	5	1983	1	3.5 y	Well
4	7	1983	4	3 mo	Died (airway problems)
5	11	1983	4	No reop	Well
6	3	1983	4	No reop	Well
7	0.25	1984	1	4 mo	Died (airway problems)
8	2.5	1984	4	6.5 y	Asthma
9	8	1984	4	5.5 y	Asthma
10	3	1985	4	No reop	Well
11	6	1985	4	No reop	Well
12	4	1986	4	No reop	Well
13	0.25	1986	3	No reop	Died (pneumonia, renal failure)
14	0.5	1987	4	2 y	Well
15	14	1987	4	No reop	Well
16	6	1988	4	No reop	Well
17	0.75	1989	4	No reop	Well
18	3	1990	4	2 mo	Well
19	12	1991	4	No reop	Well

[a] The types of operation were as follows: 1 = pulmonary aneurysmorrhaphy only; 2 = pulmonary aneurysmorrhaphy and transventricular ventricular septal defect (VSD); 3 = pulmonary aneurysmorrhaphy, transventricular VSD closure, and transannular patch; and 4 = pulmonary aneurysmorrhaphy, transatrial VSD closure, and transannular patch.

The various operative strategies are shown in Table 1. Pulmonary artery aneurysmorrhaphy has been described previously [9]. The essential features are as follows: (1) shortening of the main PA by posterior plication to lift the bifurcation area away from the trachea and draw the orifice of the right PA inferiorly, (2) posterior wall plication of the right and left PAs, and (3) anterior wall resection of the main and branch PAs. Currently, posterior wall plication of the main PA has been superseded by transection of that artery with excision of PA wall to achieve shortening of the main PA.

In those patients undergoing VSD closure and infundibular resection, the approach evolved during the course of this series from transventricular (n = 3) to transatrial (n = 14). Fifteen patients had an associated transannular incision and homograft monocusp patch (n = 2), autologous pericardial monocusp patch (n = 3), or autologous main PA wall patch (n = 10). Two who underwent transventricular VSD closure and infundibular resection did not have a transannular patch, and 2 patients with a balanced pulmonary to systemic flow ratio underwent pulmonary aneurysmorrhaphy only.

Associated cardiac lesions requiring treatment were anomalous left PA (detached from the upper descending aorta and reimplanted into the PA) and right lower lobe sequestration (aortopulmonary collateral ligation). The double aortic arch was left undisturbed because preoperative airway studies had not identified it as the offending lesion, although currently we would advise division of the minor arch in such a case.

Results

Initial Procedure

All 19 infants left the operating theater with good hemodynamics, and 16 were discharged from the hospital. The operative mortality rate was 16% (70% confidence limits, 7% to 29%). Three patients, all ventilated preoperatively, could not be weaned postoperatively because of persisting severe airway obstruction, confirmed by cinetracheobronchography. Two of these children were premature (1.7 kg and 2.3 kg) and were seen in the first days of life with severe airway obstruction requiring assisted ventilation and operation in the first week of life. The smallest (patient 13) of these 2 infants had severe persistent tracheobronchomalacia, finally complicated by sepsis and renal failure, and died 12 days postoperatively.

The second premature infant (patient 7) underwent reoperation 10 weeks after the first procedure. The main and branch PAs were excised and replaced with 10-mm Gore-Tex conduits from the right and left PA stumps to the right ventricular outflow tract on each side of the aorta. This was unsuccessful in relieving airway obstruction, and an anterior tracheobronchopexy was performed the following week. Some transient improvement was noted after this procedure, but repeat bronchography revealed persistent tracheobronchomalacia. A further bronchopexy was performed, but distal airway obstruction persisted, and the patient died 5 months after the initial procedure.

The third patient who could not be weaned postoperatively (patient 4) underwent repeat sternotomy and anterior bifurcation tracheopexy 3 months after the initial operation. Obstruction persisted, and the patient eventually died. Postmortem examination revealed a diffusely hypoplastic bronchial tree with almost complete absence of cartilage. In retrospect, this patient had a pathological condition that was not amenable to intracardiac repair and PA aneurysmorrhaphy.

Overall, 5 of the 8 patients who were ventilator dependent preoperatively survived (mortality rate, 38%; 70% confidence limits, 18% to 61%).

Long-Term Follow-up

Sixteen patients survived the initial hospitalization, and there has been only one late death (see Table 1). The first patient in the series died at reoperation 6 months after the initial procedure. Postoperative catheterization had revealed a small residual VSD and high left PA pressures. The patient could not be weaned from cardiopulmonary bypass. Postmortem examination revealed a previously undetected obstruction of the right PA caused by acute angulation at its takeoff from the main PA, which in this case had not been shortened.

All 15 long-term survivors have had regular follow-up examinations using echocardiography, with additional cardiac catheterization in 12 patients. Range of follow-up is 3 months to 11 years. Five of these patients have undergone reoperation (see Table 1). Patient 3 underwent reoperation 3½ years after the original procedure to close a previously unrepaired VSD. Patient 8 had residual left PA stenosis with major pulmonary incompetence and right ventricular dilatation. He had a reoperation at 6½ years for pulmonary homograft conduit insertion and relief of the stenoses. Patients 9 and 18 required reoperation at 5.5 years and 2 months, respectively, for relief of residual airway compression from large branch left PAs. Patient 14 had a left PA arising from the aorta and was reoperated on after 2 years for a dilated right PA beyond a proximal right PA stenosis with associated mild compression of the right main bronchus.

In the 15 survivors pulmonary incompetence is present but currently well tolerated. In 2 patients the right ventricle is dilated but contracting well. In 7 the right ventricular size is within normal limits. In 5 of these 7 there is additional mild right ventricular outflow tract obstruction.

Eight patients have episodic bronchospasm of mild to moderate severity, both isolated and in association with respiratory tract infections. All apparently obtain symptomatic relief with bronchodilators. These episodes have tended to lessen with time. The remaining 7 survivors are asymptomatic.

Comment

Absent pulmonary valve syndrome has two basic modes of presentation [3, 8, 10]. In the older, minimally symptomatic group, elective operation carries a risk similar to that of tetralogy of Fallot. In the infant group, usually symptomatic because of progressive severe airway obstruction, operation carries a higher risk. This review has focused on the latter group.

The hospital mortality of 16% (70% confidence limits, 7% to 29%) represents 3 patients, 2 of whom were premature. Both survived initial operation with good hemodynamics but died of airway complications. This has led us to question the value of our current surgical strategy in very small infants who appear to have "softer" than normal airways and are seen with life-threatening airway obstruction at birth. Palliative procedures such as PA banding or PA ligation with shunt insertion may be worth considering, although they have had variable results [11–13].

Intrapulmonary abnormalities other than direct airway compression by primary PA branches have previously been reported. In a pathological study [14], dilatation of peripheral PA vasculature and compression of intrapulmonary bronchi with consequent distal bronchomalacia was noted. Patients needing ventilatory support soon after birth may represent the severe end of this spectrum with marked peripheral bronchomalacia. At present, a direct surgical attack at this level is not possible. Consequently, many patients will be left with residual compression of small airways despite palliation at the main bronchial level (as is likely to occur after aneurysmorrhaphy). The majority of infants in this series have not fallen into this category and have exhibited a curious period of 1 month to 6 months during which airway obstruction is not immediately life threatening.

Perhaps because of the rarity of this lesion, debate has continued regarding both the etiology in and the appropriate surgical strategy for the infant group. It has been postulated that in utero closure of the ductus in absent pulmonary valve syndrome leads to increased pulmonary flow through an immature PA [15, 16]. The role of pulmonary incompetence has also been emphasized, and some published series [7, 8, 17, 18] of absent pulmonary valve syndrome have suggested that the interposition of a pulmonary valve is important to achieve early survival and relief of airway compression. This recommendation is not supported by our series, in which none of the infants had insertion of a pulmonary valve during the initial operation (although monocusp onlay patches were placed in some).

The essential component of our surgical strategy to relieve airway obstruction has been extensive PA aneurysmorrhaphy, as has been suggested by others [9, 19]. We believe this to be more important than establishing pulmonary valvar competence, at least in the short term. The aneurysmorrhaphy must incorporate shortening of the main PA to lift the PA bifurcation and proximal right PA away from the lower trachea and upper main bronchi. The reduction in diameter of the central PA system will, for a given intraluminal pressure, reduce the PA wall tension. The "hardness" of the PA (as "felt" by the main bronchi) is the PA wall tension. In the majority of infants treated on these principles, there was substantial relief of airway obstruction. The method was unsuccessful in 2 premature neonates with severe airway obstruction soon after birth and in a 7-month-old infant with distal hypoplasia of the bronchial tree, which also was largely unsupported by cartilage.

The insertion of a pulmonary valve may not be necessary for a successful outcome, although valve insertion may be required at a later date because of long-term effects of free pulmonary incompetence on the right ventricle. This has been the case in only 1 of our patients to date, although at least 2 others with free pulmonary incompetence and mild right ventricular dilatation are expected to require pulmonary valve insertion at a later date. The reoperation rate in this series has been rather high, although the condition of most patients was improved afterward. Some of these patients would currently be candidates for balloon catheter interventions, and we now would close all VSDs at the time of PA repair. Whether or not valve insertion at the time of primary operation can further reduce this incidence is unclear. Certainly a small conduit will need to be replaced at least once in long term survivors, generating further reoperations. A selective approach to primary valve insertion is probably justified at this time, with aneurysmorrhaphy as the primary treatment.

References

1. Macartney F, Miller G. Congenital absence of the pulmonary valve. Br Heart J 1970;32:483–90.
2. Lakier J, Stanger P, Heymann M, Hoffman J, Rudolph A. Tetralogy of Fallot with absent pulmonary valve: natural history and hemodynamic considerations. Circulation 1974; 50:167–75.
3. Fischer D, Neches W, Beerman L, et al. Tetralogy of Fallot with absent pulmonic valve: analysis of 17 patients. Am J Cardiol 1984;53:1433–7.
4. McCaughan B, Danielson G, Driscoll D, McGoon D. Tetralogy of Fallot with absent pulmonary valve. Early and late results of surgical treatment. J Thorac Cardiovasc Surg 1985; 89:280–7.
5. Venables AW. Absence of the pulmonary valve with ventricular septal defect. Br Heart J 1962;24:293–6.
6. D'Cruz I, Arcilla R, Agustsson M. Dilatation of the pulmonary trunk in stenosis of the pulmonary valve and of the pulmonary arteries in children. Am Heart J 1964;68:728–40.
7. Karl T, Musumeci F, de Leval M, Pincott M, Taylor JFN, Stark J. Surgical treatment of absent pulmonary valve syndrome. J Thorac Cardiovasc Surg 1986;91:590–7.
8. Ilbawi M, Idriss F, Muster A, Wessel H, Paul M, DeLeon S. Tetralogy of Fallot with absent pulmonary valve. J Thorac Cardiovasc Surg 1981;81:906–15.
9. Stellin G, Jonas RA, Goh TH, Brawn WJ, Venables AW, Mee RBB. Surgical treatment of absent pulmonary valve syndrome in infants: relief of bronchial obstruction. Ann Thorac Surg 1983;36:468–75.
10. Mavroudis C, Turley K, Stanger P, Ebert P. Surgical management of tetralogy of Fallot with absent pulmonary valve. J Cardiovasc Surg (Torino) 1983;24:604–9.
11. Byrne JP, Hawkins JA, Battiste CE, Khoury GH. Palliative procedures in tetralogy of Fallot with absent pulmonary valve: a new approach. Ann Thorac Surg 1982;33:499–502.
12. Ilbawi M, Fedorchik J, Muster A, et al. Surgical approach to severely symptomatic newborn infants with tetralogy of Fallot and absent pulmonary valve. J Thorac Cardiovasc Surg 1986;91:584–9.
13. Mocellin R, Henglein D, Beitzke A, Ahmedi A, Suppan C, Rigler B. Successful treatment of the absent pulmonary valve syndrome by banding of the pulmonary trunk. Int J Cardiol 1989;22:241–7.
14. Rabinovitch M, Grady S, David I, et al. Compression of intrapulmonary bronchi by abnormally branching pulmonary arteries associated with absent pulmonary valves. Am J Cardiol 1982;50:804–13.
15. Emmanouilides GC, Thonopoulos B, Siassi B, Fishbein M. Agenesis of ductus arteriosus associated with the syndrome of tetralogy of Fallot and absent pulmonary valve. Am J Cardiol 1976;37:403–7.
16. Callan NA, Kan JS. Prenatal diagnosis of tetralogy of Fallot with absent pulmonary valve. Am J Perinatol 1991;8:15–7.
17. Layton CA, McDonald A, McDonald L, et al. The syndrome of absent pulmonary valve. Total correction with aortic valvular homografts. J Thorac Cardiovasc Surg 1972;63: 800–8.
18. Snir E, de Leval MR, Elliott MJ, Stark J. Current surgical technique to repair Fallot's tetralogy with absent pulmonary valve syndrome. Ann Thorac Surg 1991;51:979–82.
19. Dunnigan A, Oldham HN, Benson DW Jr. Absent pulmonary valve syndrome in infancy: surgery reconsidered. Am J Cardiol 1981;48:117–22.

Effect of Delay in Retroperfusion Therapy on Infarct Size Reduction

Christopher M. Feindel, MD, Reena Sandhu, MSc, Jorge Cruz, MD, and
Gregory J. Wilson, MSc, MD

Cardiovascular Surgical Research Laboratory, Department of Cardiovascular Surgery, Toronto Western Division, Toronto Hospital Corporation, Toronto, Ontario, Canada

Retroperfusion of arterial blood through the coronary sinus reduces infarct size if therapy starts immediately after coronary artery occlusion. To determine if a new system of non–electrocardiogram-synchronized retroperfusion is able to reduce infarct size after delays consistent with clinical use, anesthetized pigs were subjected to 4 hours of left anterior descending coronary artery occlusion followed by 1 hour of reperfusion. Retroperfusion of arterial blood commenced immediately after occlusion of the left anterior descending coronary artery in the no-delay group (n = 10) and after a 1-hour (n = 10) and a 2-hour (n = 8) delay in two other groups. In the control group (n = 10), no therapy was used. In all groups, retroperfusion of arterial blood was terminated after 4 hours of occlusion of the left anterior descending coronary artery. Infarct size, expressed as a percentage of the in vivo area at risk (± the standard deviation), was smaller in the no-delay group (44.1 ± 12.9) and marginally smaller in the 1-hour delay group (71.0 ± 9.8) compared with controls (86.3 ± 7.5) ($p < 0.05$). Infarct size in the 2-hour delay group (75.0 ± 10.7) was not significantly different from controls. Mean coronary sinus pressure (± the standard deviation) was 56 ± 25 mm Hg, 39 ± 9 mm Hg, and 47 ± 9 mm Hg in the no-delay, 1-hour delay and 2-hour delay groups, respectively. Thus, this new retroperfusion system limits infarct size by 50% if it is started immediately after coronary occlusion. However, if institution of retroperfusion is delayed, only marginal benefit is achieved in a model of minimal intercoronary collateralization.

(Ann Thorac Surg 1992;54:1120–5)

In the last 15 years, numerous experimental studies have demonstrated that retrograde administration of arterial blood through the coronary sinus is effective in reducing myocardial infarct size [1–3] and improving cardiac function [1, 4–9] when therapy is applied at the time of experimental coronary artery occlusion. Although application of therapy at the time of occlusion represents a situation where optimal benefit can be demonstrated, it does not represent the realistic delays that can occur between the onset of symptoms and the administration of therapy in patients with acute myocardial infarction.

The purpose of this study was to define the time window within which arterial retroperfusion must be applied after a coronary occlusion to salvage ischemic myocardium. The intermittent coronary sinus retroperfusion (ICSR) system we tested differs from the electrocardiogram-synchronized system developed by Meerbaum and co-workers [4] and previously investigated in that retroperfusion is not limited to diastole but occurs over a period of several cardiac cycles, typically during inflation of a coronary sinus balloon catheter, followed recurrently by a period of no retroperfusion when the coronary sinus balloon catheter is deflated.

Presumably, coronary venous retroperfusion works by creating a temporary obstruction in the coronary venous system. This results in the development of a pressure gradient, which forces the actively retroperfused arterial (ie, well-oxygenated) blood into the ischemic zone where it can serve as nutritional support.

The present study was conducted in the pig, an animal with few intercoronary collaterals [10–12], because there is a subset of patients who have few, if any, angiographically demonstrated collaterals [13]. As the amount of collateral flow is a critical determinant of myocardial infarct size [10, 14–16], it is assumed that in the pig model with minimal collateralization, we are defining a lower time limit for delaying the implementation of ICSR, a limit still effective in limiting infarct size.

Material and Methods

The ICSR System

The ICSR device (supplied by Rocky Mountain Research Inc, Salt Lake City, UT) used in this study has two major components: a controller and a delivery device that is connected to a 16F triple-lumen balloon-tipped coronary sinus catheter (Fig 1). The delivery system uses a miniature roller pump driven by a direct-current stepping motor to provide perfusion to the central lumen of the catheter. A solenoid-actuated syringe is used to inflate and deflate the balloon on the tip of the coronary sinus catheter. The third lumen of the catheter is connected to a pressure transducer and is used to monitor coronary sinus

---

Accepted for publication March 23, 1992.

Address reprint requests to Dr Feindel, Department of Cardiovascular Surgery, Rm 14-222, Eaton Wing, The Toronto General Hospital, 200 Elizabeth St, Toronto, Ont, Canada M5G 2C4.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

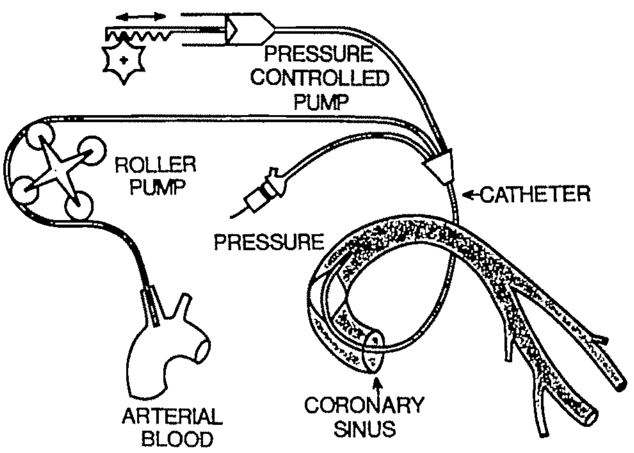


Fig 1. Intermittent coronary sinus retroperfusion system (generously supplied by Rocky Mountain Research Inc, Salt Lake City, UT).

pressure. The controller allows both the inflation and deflation times of the balloon to be adjusted independently between 0 and 99 seconds and the roller pump speed to be set to deliver blood at rates ranging from 0 to 600 mL/min. Perfusion can be set to run continuously or only in the inflation part of the cycle, as desired.

Experimental Preparation

Yorkshire pigs weighing 24 to 34 kg were initially sedated with ketamine hydrochloride (30 mg/kg). After endotracheal intubation, they were anesthetized and ventilated by a Narco Air-Shield ventilator on a Boyle anesthetic machine delivering a mixture of oxygen (80%), nitrous oxide (20%), and isoflurane (0.75% to 1.5%). The left ear vein was catheterized for administration of intravenous fluids. A midline sternotomy and pericardiotomy were performed to expose the heart and great vessels of the neck.

A catheter inserted into the left carotid artery was used for monitoring arterial pressure and for sampling blood. A catheter placed in the innominate artery was connected through the roller pump of the retroperfusion device to the central lumen of the coronary sinus catheter to serve as the source of arterial blood. A triple-lumen thermodilution catheter (American Edwards Laboratories) was positioned in the pulmonary artery through the left jugular vein to determine cardiac output. A triple-lumen balloon-tipped Foley catheter (16F 50-mL balloon; Reich of Canada) was manually advanced into the orifice of the coronary sinus through the superior vena cava. The catheter was positioned such that the balloon was approximately 0.5 cm inside the coronary sinus. Correct positioning of the catheter was confirmed periodically throughout the experiment by manual palpation and direct visualization. Because the left hemiazygos vein empties into the proximal coronary sinus in the pig, it was necessary to ligate this vein to prevent the retroperfusate from escaping through this route.

The left anterior descending coronary artery (LAD) was dissected at the level of the second diagonal branch with great care taken to prevent damage to the accompanying coronary veins. After a period of stabilization, lidocaine hydrochloride (50 mg) and heparin sulfate (10,000 U) were administered intravenously. The LAD was occluded for 4 hours with a silk ligature, and then the ligature was released to allow 1 hour of reperfusion. Hemodynamic measurements (heart rate, arterial pressure, coronary sinus pressure, and cardiac output) were measured before occlusion, and these measurements were repeated 120, 230, and 290 minutes after occlusion.

The animals were treated humanely in compliance with the "Guide to the Care and Use of Experimental Animals," volume 1 (1980) and volume 2 (1984), Canadian Council on Animal Care.

Study Protocol

The animals were divided into four groups based on when retroperfusion of arterial blood was begun. In all four groups, the LAD was occluded for 4 hours and then reperfused for 1 hour. In the no-delay group, ICSR commenced immediately after coronary occlusion and continued until the end of the 4-hour occlusion period. In the 1-hour and 2-hour delay groups, ICSR commenced 1 hour and 2 hours after coronary occlusion, respectively, and also continued until the end of the 4-hour occlusion period. In the control group, no therapy was given (no coronary sinus catheter), but the left hemiazygos vein was ligated. Intermittent coronary sinus retroperfusion consisted of 5 seconds of balloon inflation followed by 5 seconds of balloon deflation with retroperfusion of arterial blood at 60 mL/min during the inflation part of the cycle.

Determination of Area at Risk and Infarct Size

The area at risk of infarction was delineated at the end of the reperfusion period by again occluding the LAD at the previous ligation site and injecting 1 million radioactive microspheres, 15 ± 3 μm in diameter and labeled with cerium 141 (Dupont-NEN, Montreal, Que), into the left atrium over a 1-minute period. The microspheres were suspended in 10 mL of 0.9% sterile saline solution containing 0.01% Tween 80. One hour after reperfusion, the animals were killed with an overdose of isoflurane and potassium chloride. The hearts were excised, sliced transversely into sections 1 cm thick, weighed, and assessed for necrosis by incubation in tetrazolium chloride according to the method of Lie and colleagues [17]. Tetrazolium-positive tissue (dark red) was considered viable, whereas areas that failed to stain with tetrazolium (pale) were considered necrotic.

Each slice was then sandwiched gently between transparent plates to hold it in a fixed orientation. Care was taken to prevent tissue distortion when placing the heart slices into the device. The heart slices were photographed on both sides using 10 × 15-cm Kodak Ektachrome 64T tungsten film. This film produces color transparencies showing the actual size of heart slices. These transparencies were used for later planimetric assessment of infarct size. Autoradiographs were then made by placing Kodak X-Omatic x-ray film on each side of the slice and exposing the film for 48 hours at 4°C. After it was developed, the exposed film was carefully aligned with the original full-format heart photograph. Correct alignment of the heart slices was facilitated by the placement of small metallic markers on the transparent plates. As these markers were visible on both the photographs and the autoradiographs, they served for the alignment of the two sheets. Once developed, the x-ray film revealed the extent of trapping of the ^{141}Ce-tagged microspheres and thus delineated the area at risk at the time of microsphere injection (ie, 1 hour after reperfusion of the LAD).

The outlines of the area at risk, the area infarcted, and the area occupied by the left and right ventricles were analyzed by computerized planimetry. By using the mass of each slice, the percentage of necrotic myocardium within the area at risk was calculated for each heart as described previously [18].

Statistical Analysis

All values are expressed as the mean ± one standard deviation. All data first were analyzed to determine if the assumptions for parametric testing (normal distributions and equal variances) were met. Because they were met, a one-way analysis of variance was used to compare area at risk and infarct sizes between the four groups. The Scheffé *F* test was employed to determine which differences were significant. Hemodynamic data were analyzed using an analysis of variance for repeated measures. Deaths caused by ventricular fibrillation were compared between the four groups using Fisher's exact test. Significance was defined as a p value of less than 0.05.

Results

There were no significant differences in the mean values for body weight and left ventricular weight between the four experimental groups.

Exclusions

Of the 52 pigs initially entered into the study, 13 did not complete the protocol. Two animals died during the surgical procedure owing to technical difficulties associated with LAD dissection. Two pigs in the 2-hour delay group were excluded from the study because of technical complications with the autoradiograms. Two animals died of ventricular fibrillation within the first few minutes of coronary occlusion before they were assigned to a group. A further 6 pigs (2 in the no-delay group and 2 each in the 1-hour and 2-hour delay groups) died of ventricular fibrillation within the first 30 minutes of retroperfusion therapy. One pig in the 2-hour delay group died minutes after reperfusion had begun. There were no deaths caused by ventricular fibrillation in the control group. Thus, 2, 2, 3, and 0 deaths were due to ventricular fibrillation in the no-delay, 1-hour delay, 2-hour delay, and control groups, respectively. The number of deaths due to ventricular fibrillation was not significantly different between the four groups ($p = 0.44$, Fisher's exact test).

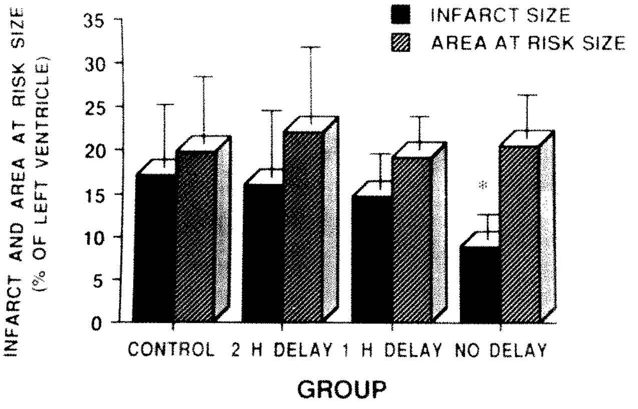


Fig 2. Comparison of infarct and area-at-risk sizes expressed as percentage of the left ventricle between the four groups. (p < 0.05 versus control group by Scheffé test.)*

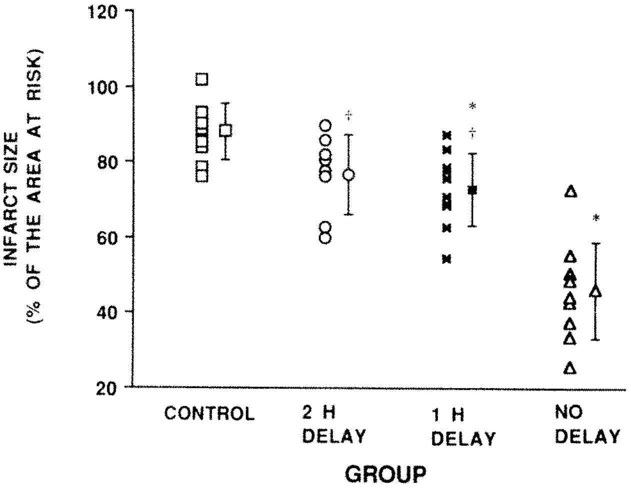


Fig 3. Comparison of percentage of area at risk infarcted between the four groups. (p < 0.05 versus control group by Scheffé test; † p < 0.05 versus no-delay group by Scheffé test.)*

Infarct Size

Figure 2 shows the infarct and area-at-risk sizes expressed as a percentage of the left ventricle. The microsphere-determined area at risk, as measured at the end of the experiment, was nearly identical in the four groups. Infarct size, when considered as a percentage of the left ventricle, was significantly smaller only in the no-delay group compared with controls ($p < 0.01$). The percentage of the area at risk that was infarcted was 44.1% ± 12.9% in the no-delay group, 71.0% ± 9.8% in the 1-hour delay group, 75.0% ± 10.7% in the 2-hour delay group, and 86.3% ± 7.5% in the control group, which received no retroperfusion therapy (Fig 3). When comparisons were made with the control group, application of retroperfusion reduced infarct size as expressed as a percentage of the area at risk in the no-delay group ($p < 0.001$) and the 1-hour delay group ($p = 0.03$). The administration of ICSR therapy after a 2-hour delay did not significantly reduce infarct size ($p = 0.06$). Immediate commencement of retroperfusion (no delay) achieved significantly greater

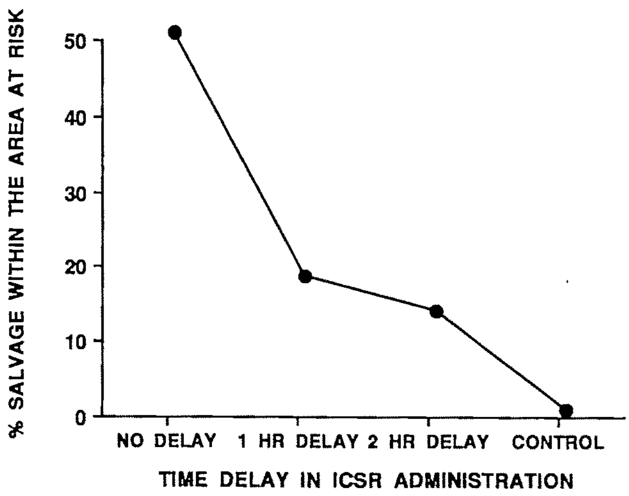


Fig 4. Relationship between delay in administration of intermittent coronary sinus retroperfusion (ICSR) and percentage of the area at risk salvaged.

salvage than that achieved after a 1-hour or 2-hour delay ($p < 0.001$). Immediate application of ICSR resulted in a 50% reduction in infarct size; however, the amount of myocardium salvaged by ICSR falls to 17% and 11% after delays in administration of 1 hour and 2 hours, respectively (Fig 4).

Macroscopically, infarcts in the control, 1-hour, and 2-hour delay groups appeared as confluent areas, whereas in the no-delay group, they appeared as small, patchy areas interspersed among salvaged tissue. A few animals in each of the retroperfused groups exhibited small hemorrhagic areas within the myocardium. In all cases, these areas were confined to the borders of the infarct.

Hemodynamics

The hemodynamic data for the four experimental groups are summarized in Table 1. Two-way analysis of variance for repeated measures revealed a significant time effect for each of the hemodynamic variables ($p < 0.0001$). However, there was no significant group effect for any of these variables, indicating that the changes across time in the control group were not different from the corresponding changes across time in the retroperfused groups.

Mean coronary sinus pressure was 56.1 ± 25.4 mm Hg, 38.0 ± 8.5 mm Hg, and 47.3 ± 8.9 mm Hg in the no delay, 1-hour delay, and 2-hour delay groups, respectively. Throughout the entire 4-hour occlusion period, coronary sinus pressures promptly fell to a right atrial pressure level immediately on balloon deflation in all three groups receiving retroperfusion, indicating that the coronary sinus had not thrombosed while the catheter was in position. Mean coronary sinus pressure was higher in the no-delay group compared with the 1-hour delay group, but this did not quite reach significance ($p = 0.052$).

Comment

This study demonstrates that retroperfusion with arterial blood is able to salvage ischemic myocardium in animals with minimal collateralization. However, time of initiation of therapy was of critical importance in obtaining a beneficial effect, as initiation of retroperfusion immediately after coronary occlusion produced substantially more salvage than did administration delayed for 1 hour or 2 hours after occlusion.

The amount of myocardium available for salvage by the application of retroperfusion after a 1-hour or 2-hour delay depends on (1) the effectiveness of retroperfusion in salvaging ischemic myocardium and (2) how much of the myocardium within the area at risk has already under-

Table 1. Hemodynamic Data for the Four Experimental Groups[a]

Variable	Control	No Delay	1-Hour Delay	2-Hour Delay
Mean arterial pressure (mm Hg)				
Before occlusion	83.7 ± 10.4	81.7 ± 7.3	92.5 ± 10.0	87.4 ± 10.4
120 minutes after occlusion	67.7 ± 10.7	69.7 ± 11.0	72.2 ± 18.8	67.6 ± 11.6
230 minutes after occlusion	65.8 ± 8.4	68.1 ± 12.1	57.7 ± 13.2	69.0 ± 16.0
290 minutes after occlusion	61.5 ± 6.6	63.4 ± 14.7	57.9 ± 13.5	56.8 ± 16.6
Heart rate (beats/min)				
Before occlusion	111.4 ± 8.6	107.0 ± 9.2	108.7 ± 14.2	106.5 ± 10.2
120 minutes after occlusion	100.9 ± 8.7	101.7 ± 7.2	95.3 ± 8.8	99.0 ± 7.0
230 minutes after occlusion	99.8 ± 7.4	100.2 ± 6.4	98.0 ± 19.0	92.6 ± 14.2
290 minutes after occlusion	99.1 ± 5.7	100.3 ± 4.3	104.0 ± 17.3	90.5 ± 15.0
Rate–pressure product (beats × mm Hg/min)				
Before occlusion	11,492.8 ± 1,440.1	11,222.5 ± 1,502.2	12,088.0 ± 1,973.8	11,492.8 ± 1,440.2
120 minutes after occlusion	9,057.6 ± 1,631.6	9,327.6 ± 1,097.1	8,552.3 ± 1,859.9	8,840.9 ± 1,636.5
230 minutes after occlusion	8,672.1 ± 1,435.7	8,949.7 ± 956.2	7,292.7 ± 1,216.2	8,453.6 ± 2,576.2
290 minutes after occlusion	8,422.0 ± 1,170.8	8,593.4 ± 1,198.6	7,928.0 ± 1,172.2	7,197.0 ± 2,174.2

[a] For each of the hemodynamic variables, repeated-measures analysis of variable indicated a significant time effect ($p < 0.001$); however, there were no significant group effects ($p < 0.05$) for any of the hemodynamic variables measured.

gone necrosis by the time retroperfusion is applied. Schaper and co-workers [14] documented that the rate of infarct development in the pig is rapid: more than 90% of the area at risk is necrotic after 45 minutes of coronary occlusion, and maximal infarct size is achieved after 90 minutes of occlusion. These results are similar to those of Fujiwara and associates [16] and suggest that the time window in which any therapy can potentially demonstrate a beneficial effect in the pig model is very small, perhaps less than 45 minutes in a situation of minimal collateralization. However, Horneffer and co-authors [19] observed that only 43% and 71% of the area at risk was infarcted in the pig after 45 and 90 minutes of occlusion, respectively. They noted that infarction was still occurring up to 180 minutes of occlusion, which suggests that the time window for therapeutic intervention in this species may be larger than that proposed by Schaper [14], Fujiwara [16], and their associates. Other investigators [10, 20–22] also observed a slower rate of infarct progression with approximately 60% or less of the area at risk being infarcted after periods of occlusion of 60 minutes or longer. The difference between the rates of infarct progression in these studies may be attributed to several factors including differences in myocardial oxygen consumption, collateral flow, length of the reperfusion period, and differences in the size of the area at risk.

In the current investigation, the observation that retroperfusion was able to salvage myocardium after a 1-hour delay suggests that noninfarcted myocardium was still present at this time in this model of minimal intercoronary collateralization, and that consequently, the rate of infarct progression was slower in this study compared with that of Fujiwara and co-workers [16] or Schaper and colleagues [14]. This may have been due to the lower myocardial oxygen consumption in the present study, as the product of rate times pressure (an indicator of myocardial oxygen demand) fell significantly in all experimental groups during the occlusion and reperfusion periods. The importance of myocardial oxygen consumption and hemodynamics on ultimate infarct size has been previously examined in the pig [14, 20] and is known to play a role in governing the rate at which an infarct evolves. The reason for the declines in the measured hemodynamic variables cannot be determined from these experiments. However, there was no significant group effect for any of the hemodynamic variables, indicating that all of the groups were similar in this regard.

Comparison of Retroperfusion With Reperfusion

Of all the therapies tested for salvage of ischemic myocardium, only early reperfusion has been adopted for widespread clinical use [23]. Therefore, if reperfusion is used as the gold standard by which to compare the efficacy of retroperfusion, studies initiating retroperfusion and reperfusion at comparable intervals after coronary occlusion would yield important information. Geary and associates [3] compared the degree of myocardial salvage obtained with antegrade arterial reperfusion and electrocardiogram-synchronized retroperfusion in baboons subjected to LAD occlusion and found that retroperfusion after 1 hour of coronary occlusion resulted in salvage similar to that obtained with antegrade reperfusion after 2 hours of occlusion.

The mechanisms by which retroperfusion exerts a beneficial effect on the ischemic myocardium are uncertain but are presumably related to the provision of arterial blood to the ischemic myocardium and the washout of toxic metabolites. However, it is unclear what proportion of the arterial retroperfusate actually serves as nutritional support for the ischemic myocardium and how much is simply shunted through venous anastomoses [24].

Validity of Tetrazolium Staining to Quantify Necrosis

In this investigation, myocardial infarct size was quantified using tetrazolium staining. Previous investigations in our laboratory in pigs subjected to a protocol similar to that in the no-delay group have checked tetrazolium staining against electron microscopy, as it has been suggested that tetrazolium nonstaining may not be an adequate predictor of myocardial necrosis [25]. Our studies demonstrated that in the model we have used, electron microscopy (using either conventional or a low-denaturation [26] tissue processing technique) validated the tetrazolium chloride staining technique and that areas appearing unstained using tetrazolium were clearly irreversibly damaged as exemplified by the presence of sarcolemmal disruptions and the presence of mitochondria containing multiple, large electron-dense deposits. On the other hand, areas that were stained by tetrazolium (tetrazolium-positive-red) appeared either normal or only mildly ischemic. We are confident, therefore, that the tetrazolium staining used in this study provided an adequate end point for the identification of areas of necrosis.

Clinical Implications

In a clinical setting, it is important to know when the application of retroperfusion therapy is no longer likely to be effective in limiting infarct size. We have demonstrated that in an animal with minimal collateralization, ICSR results in only modest salvage of ischemic myocardium if it is instituted after delays of an hour or more. However, patients with acute myocardial infarction show a great deal of variability in the extent of preformed collaterals and, as a result, a great deal of variability in the rates at which an infarct will evolve. Thus, it is possible that patients with extensive preformed collaterals may benefit from the effects of retroperfusion for longer periods after coronary occlusion.

The finding that the ICSR system reduced infarct size substantially in the no-delay group supports the potential use of this system in an emergency "bail-out" procedure for abrupt coronary closure during percutaneous transluminal coronary angioplasty. Because a coronary sinus catheter can be placed within minutes and with little difficulty, the possible use of the ICSR system in this situation needs to be investigated.

The ICSR system offers some advantages over the electrocardiogram-synchronized system, which has been previously reported [1–9]. First, because the system does not synchronize to the electrocardiogram, it is compact and inexpensive and can be easily transported with a patient. Second, difficulties in tracking the heart beat, which are particularly great in the presence of arrhythmias, are avoided. A potential disadvantage of the ICSR system is the presence of high coronary sinus pressures that are maintained over several cardiac cycles unlike in the synchronized system, in which the elevated coronary sinus pressures are relieved during each systole.

Additional studies are needed to optimize the ICSR system. They should determine the coronary sinus pressures and the occlusion/release cycles needed for myocardial protection.

This work was generously supported by grant AN429 from the Ontario Heart and Stroke Foundation.

We gratefully acknowledge Ms Patty Boylen for technical assistance.

References

1. Farcot JC, Meerbaum S, Lang T, Kaplan L, Corday E. Synchronized retroperfusion of coronary veins for circulatory support of jeopardized ischemic myocardium. Am J Cardiol 1978;41:1191–201.
2. Smith GT, Geary GG, Blanchard W, McNamara JJ. Reduction in infarct size by synchronized selective coronary venous retroperfusion of arterialized blood. Am J Cardiol 1981;48: 1064–70.
3. Geary GG, Smith GT, Suehiro GT, Zeman C, Siu B, McNamara JJ. Quantitative assessment of infarct size reduction by coronary venous retroperfusion in baboons. Am J Cardiol 1982;50:1424–30.
4. Meerbaum S, Lang TW, Osher JV, et al. Diastolic retroperfusion of acutely ischemic myocardium. Am J Cardiol 1976; 37:588–98.
5. Yamazaki S, Drury JK, Meerbaum S, Corday E. Effects of synchronized retroperfusion on left ventricular function measured by two dimension echocardiography. In: Mohl W, Wolner E, Glogar D, eds. The coronary sinus. Darmstadt: Steinkopff Verlag, 1984:375–9.
6. Gundry SR. Modification of myocardial ischemia in normal and hypertrophied hearts utilizing diastolic retroperfusion of the coronary veins. J Thorac Cardiovasc Surg 1982;83:659–69.
7. Yamazaki S, Drury JK, Meerbaum S, Corday E. Synchronized coronary venous retroperfusion: prompt improvement of left ventricular function in experimental myocardial ischemia. J Am Coll Cardiol 1985;5:655–63.
8. Farcot JC, Berdeaux A, Guidicelli JF, Vilaine JP, Bourdarias JP. Diastolic synchronized retroperfusion versus reperfusion: effects on regional left ventricular function and myocardial blood flow during acute coronary occlusion in dogs. Am J Cardiol 1983;51:1414–21.
9. Morkov AK, Lehan PH, Hellems HK. Reversal of acute myocardial ischemia in closed chested animals by retrograde perfusion of the coronary sinus with arterial blood. Acta Cardiol (Brux) 1976;185–99.
10. Savage RM, Guth B, White FC, Hagan AD, Bloor CM. Correlation of regional myocardial blood flow and function with myocardial infarct size during acute myocardial ischemia in the conscious pig. Circulation 1981;64:699–707.
11. Maxwell MP, Hearse DJ, Yellon DM. Species variation in the coronary collateral circulation during regional myocardial ischemia: a critical determinant of the rate of evolution and extent of myocardial infarction. Cardiovasc Res 1987;21: 737–46.
12. Hearse DJ, Muller CA, Fukanami M, Kudoh Y, Opie LH, Yellon DM. Regional myocardial ischemia: characterization of temporal, transmural and lateral flow interfaces in the porcine heart. Can J Cardiol 1986;2:48–61.
13. Dewood MA, Heit J, Spores J, et al. Anterior transmural myocardial infarction: effects of surgical coronary reperfusion on global and regional left ventricular function. J Am Coll Cardiol 1983;1:1223.
14. Schaper W, Binz K, Sass S, Winkler B. Influence of collateral blood flow and of variations in MVO2 on tissue-ATP content in ischemic and infarcted myocardium. J Mol Cell Cardiol 1987;19:19–37.
15. Schaper W. The collateral circulation of the heart. Prog Cardiovasc Dis 1988;31:57–77.
16. Fujiwara H, Matsuda M, Fujiwara Y, et al. Infarct size and the protection of ischemic myocardium in pig, dog and human. Jpn Circ J 1989;53:1092–7.
17. Lie JT, Pairolero PC, Holley KE, Titus JL. Macroscopic enzyme mapping verification of large, homogenous experimental myocardial infarcts of predictable size and location in dogs. J Thorac Cardiovasc Surg 1975;69:599–605.
18. Feindel CM, Tait GA, Wilson GJ, Klement P, MacGregor DC. Multidose blood versus crystalloid cardioplegia. Comparison by quantitative assessment of irreversible myocardial injury. J Thorac Cardiovasc Surg 1984;87:585–95.
19. Horneffer PJ, Healy B, Gott VL, Gardner TJ. The rapid evolution of a myocardial infarction in an end-artery coronary preparation. Circulation 1987;76(Suppl 5):39–42.
20. Garcia-Dorado D, Theroux P, Elizaga J, Fernandez F, Alonso J, Solares J. Influence of tachycardia and arterial hypertension on infarct size in the pig. Cardiovasc Res 1988;22:620–6.
21. Klein HH, Schubothe M, Nebandahl K, Kreuzer H. Temporal and spatial development of infarcts in porcine hearts. Basic Res Cardiol 1983;79:440–7.
22. Warltier DC, Zyvoloski MG, Gross GJ, Brooks HL. Subendocardial versus transmural myocardial infarction: relationship to the collateral circulation in the canine and porcine hearts. Can J Physiol Pharmacol 1982;60:1700–6.
23. Reimer KA, Jennings RB. Experimental models and endpoints for evaluating interventions in the acute phase of myocardial infarction: an anatomic approach. In: Morganroth J, Moore EN, eds. Interventions in the acute phase of myocardial infarction. New York: Martinus Nijhoff, 1984: 1–11.
24. Cohen MV, Matsuki T, Downey JM. Pressure-flow characteristics and nutritional capacity of coronary veins in dogs. Am J Physiol 1988;255:H834–46.
25. Barnard RJ, Okamoto F, Buckberg GD, et al. Studies of controlled reperfusion after ischemia. III. Histochemical studies: inability of triphenyltetrazolium chloride nonstaining to define tissue necrosis. J Thorac Cardiovasc Surg 1986;92:502–12.
26. Sjostrand F, Allen BS, Buckberg GD, et al. Studies of controlled reperfusion after ischemia. IV. Electron microscopic studies: importance of embedding techniques in quantitative evaluation of cardiac mitochondrial structure during regional ischemia and reperfusion. J Thorac Cardiovasc Surg 1986;92: 513–24.

Hyperglycemia Increases Cerebral Intracellular Acidosis During Circulatory Arrest

Richard V. Anderson, MD, Michael G. Siegman, MD, Robert S. Balaban, PhD,
Toni L. Ceckler, PhD, and Julie A. Swain, MD

Surgery Branch and Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, and Department of Surgery, University of Nevada School of Medicine, Las Vegas, Nevada

Phosphorus 31 nuclear magnetic resonance spectroscopy was used to assess cerebral high-energy phosphate metabolism and intracellular pH in normoglycemic and hyperglycemic sheep during hypothermic circulatory arrest. Two groups of sheep (n = 8 per group) were placed in a 4.7-T magnet and cooled to 15°C using cardiopulmonary bypass. Spectra were acquired before and during circulatory arrest and during reperfusion and rewarming. Intracellular pH and adenosine triphosphate levels decreased during circulatory arrest. Compared with the normoglycemic animals, the hyperglycemic group was significantly more acidotic with the greatest difference observed during the first 20 minutes of reperfusion (6.40 ± 0.08 versus 6.08 ± 0.06; $p < 0.001$). Intracellular pH returned to baseline after 30 minutes of reperfusion in the normoglycemic group but did not reach baseline until 1 hour of reperfusion in the hyperglycemic animals. Adenosine triphosphate levels were significantly higher in the hyperglycemic group during circulatory arrest. Repletion of adenosine triphosphate during reperfusion was similar for both groups. These results support the hypothesis that hyperglycemia during cerebral ischemia drives anaerobic glycolysis and thus leads to increased lactate production and a decrease in the intracellular acidosis normally associated with ischemia.

(Ann Thorac Surg 1992;54:1126–30)

Hyperglycemia may develop in patients subjected to the stress of cardiac operation and hypothermic cardiopulmonary bypass (CPB). Disturbances of insulin and glucose metabolism stem from impaired insulin production, decreased glucose utilization, and increased levels of gluconeogenic hormones, such as epinephrine, cortisol, glucagon, and growth hormone [1, 2]. In addition, the use of dextrose-containing solutions for peripheral fluid administration, CPB prime, and cardioplegia delivers a substantial exogenous glucose load. In nondiabetic patients this condition is self-limiting and often goes untreated. In diabetic patients, a more profound hyperglycemia may develop, resulting in serious complications and even death [3].

See also page 1131.

During ischemia, the metabolism of glucose by anaerobic glycolysis results in lactate production and intracellular acidosis. Hyperglycemia will potentiate this reaction, resulting in increased lactate production and a further decrease in intracellular pH. During normothermic ischemia, severe acidosis increases cell damage and impairs energy metabolism after ischemia [4].

The effects of hyperglycemia during hypothermic cerebral ischemia and reperfusion have not been defined. In this study, deep hypothermic circulatory arrest was used as a model of global cerebral ischemia. We employed in vivo phosphorus 31 nuclear magnetic resonance spectroscopy (NMR) to examine the effects of hyperglycemia on intracellular pH and high-energy phosphate metabolism during ischemia and reperfusion in the sheep brain.

Material and Methods

Animal Preparation

All animal experiments were conducted with the approval of the Animal Care Use Committee of the National Heart, Lung, and Blood Institute in accordance with the "Guide for the Care and Use of Laboratory Animals" (NIH publication No. 85-23, revised 1985).

Twenty sheep weighing between 18 and 34 kg were divided into two groups (normoglycemia and hyperglycemia). Hornless sheep were used because of the relatively thin skull bone in the frontoparietal region, which reduces interference with the NMR signal. Juvenile sheep (greater than 8 weeks of age) were used because their erythrocytes lack 2,3-diphosphoglycerate, which interferes with the accurate determination of the resonance position of inorganic phosphate. The inorganic phosphate resonance position is required for the calculation of intracellular pH.

Anesthesia was induced with intravenous Telazol (1:1 tiletamine hydrochloride and zolazepam hydrochloride), 0.1 mL/2.5 kg. Endotracheal intubation was performed, and inhalation anesthesia was maintained with a mixture of 1% halothane and 99% oxygen. Muscle paralysis was

---

Accepted for publication March 23, 1992.

Presented at the Clinical Congress Surgical Forum of the American College of Surgeons, Chicago, IL, Oct 20–25, 1991.

Address reprint requests to Dr Swain, Division of Cardiovascular Surgery, University of Nevada School of Medicine, 2040 W Charleston Blvd, Suite 601, Las Vegas, NV 89102.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

obtained with intravenous administration of pancuronium bromide, 0.1 mg/kg. Arterial pressure and venous infusion catheters were placed in the right femoral artery and vein, respectively. The left femoral artery was cannulated with a 14F or 16F CPB catheter. A 24F lighthouse-tip CPB cannula was placed into the right atrium through the right internal jugular vein. Heparin sodium (300 U/kg) was administered intravenously before arterial and venous cannulation. An insulated, single-turn, custom-made radiofrequency coil 2 cm in diameter was secured over the exposed skull. The animal was then wrapped in an insulating blanket, placed in a Lucite cradle, and positioned in a 4.7-T, 30-cm clear-bore magnet.

Arterial blood oxygen tension was maintained greater than 100 mm Hg; normothermic carbon dioxide tension was maintained between 35 and 45 mm Hg. Mean arterial pressure was maintained between 60 and 90 mm Hg at 37°C and between 40 and 60 mm Hg at 15°C. Nasopharyngeal temperature was monitored with a temperature probe unaffected by the magnetic field. Serum electrolyte and glucose levels were intermittently measured using a Chem Pro 1000 Clinical Chemistry Analyzer (Ortho Diagnostic Systems Inc, Raritan, NJ).

Cardiopulmonary Bypass

The bypass circuit consisted of a centrifugal pump (model BP-80; Bio-Medicus, Eden Prairie, MN), a 33-μm arterial filter (model H-625; Bard Cardiopulmonary Division, Santa Ana, CA), and a hollow-fiber membrane oxygenator with integral heat exchanger (Maxima; Medtronic Blood Systems, Inc, Anaheim, CA). A cardiotomy reservoir (Gish Biomedical, Inc, Santa Ana, CA) was inserted parallel to the venous line for the administration of volume and as a reservoir for exsanguination of the animal during the arrest period. The pump was positioned 4.5 m from the magnet, and this necessitated corresponding lengths of extension tubing. The pump was primed with 2,500 mL of lactated Ringer's solution, 10,000 units of heparin, 50 mEq of sodium bicarbonate, 12.5 g of mannitol, 80 mg of 2% lidocaine hydrochloride, and 1 unit of sheep whole blood.

Blood flow during CPB was maintained between 60 and 100 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Flow was measured with an electromagnetic flowmeter (Bio-Medicus) that had previously been calibrated in the weak magnetic field (15 G) where the pump was positioned. The oxygenator was ventilated with a mixture of 1% halothane and 99% oxygen.

After baseline NMR spectra were acquired at 37°C for 20 minutes, the animal was cooled to 15°C. Cooling took 29 to 53 minutes. During hypothermia, the arterial blood pH was managed using the alpha-stat scheme. After spectra acquisition at 15°C for 20 minutes, circulation was arrested for 1 hour, followed by 2 hours of reperfusion and rewarming. Before reperfusion, 25 g of mannitol and a second unit of whole blood were added to the cardiotomy reservoir. Inotropic support (dopamine hydrochloride, 5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) was initiated with reperfusion in all animals. Rewarming was accomplished by maintaining a 10°C gradient between the blood and water bath temperatures. Sheep in which massive edema developed, manifested as pulmonary edema in the ventilator tubing and no return of cerebral adenosine triphosphate (ATP) levels, were unable to be weaned from bypass and were excluded from the study. Four of the 12 control animals had to be excluded for this reason. (These 4 animals required large volumes of fluid to maintain adequate flows while on CPB.) None of the hyperglycemic animals showed massive edema. Animals weaned from bypass were ventilated for the duration of the experiment. No attempt was made to wean from the ventilator. At the completion of 2 hours of reperfusion, animals were killed with intravenous administration of potassium chloride. Total time on CPB, including the arrest period, ranged from 4 hours 20 minutes to 4 hours 48 minutes.

Glucose Monitoring and Treatment

All animals fasted 12 hours before the experiment. The initial glucose level was determined as soon as venous access was obtained but before the start of maintenance fluid administration. All animals were initially normoglycemic (glucose level < 8.3 mmol/L [150 mg/dL]). The control (normoglycemic) animals received lactated Ringer's as maintenance fluid. The animals in the hyperglycemic group were administered lactated Ringer's with 5% dextrose as maintenance fluid. By the time the animals were transferred to the magnet and preparations for CPB had been completed, the animals in the treatment group had become hyperglycemic (glucose level > 13.9 mmol/L [250 mg/dL]).

Serum glucose levels were measured before initiation of CPB, during CPB at 37°C, during CPB at 15°C, during early reperfusion, and at 1 hour of reperfusion when rewarming was complete. Animals in the treatment group with glucose levels that fell to less than 13.9 mmol/L received intravenous injections of 50% dextrose in 12.5-mEq increments until the level was once again greater than 13.9 mmol/L. This was necessary on only three occasions.

NMR Spectroscopy

The techniques of NMR spectroscopy used in this study have been described previously [5]. The animal was positioned so that the brain was centered in the bore of the magnet. The NMR data were collected with a General Electric CSI spectrometer (General Electric NMR Instruments, Fremont, CA). The data were acquired in 20-minute blocks of 640 averaged acquisitions at 37°C before CPB, 37°C on CPB, and 15°C on CPB. Nine consecutive 20-minute blocks were then acquired, three during the arrest period and six during the reperfusion and rewarming period. Data were analyzed using the GEMCAP Lorentzian line-fitting program, a part of the GEMCSI software.

Concentrations of ATP and phosphocreatine (PCr) are reported as percent change from baseline levels acquired at 37°C off CPB. Intracellular pH was determined by measuring the chemical shift of the inorganic phosphate peak relative to the position of the pH-independent PCr peak. The relation between pH and inorganic phosphate

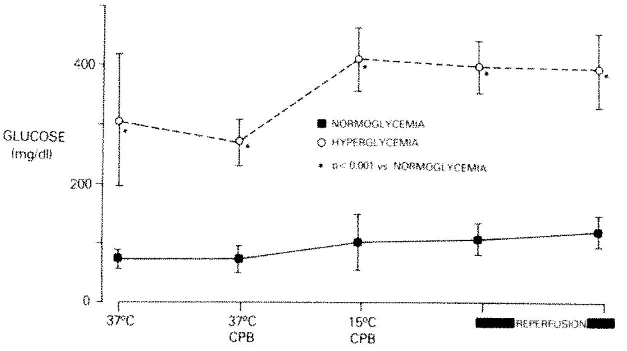


Fig 1. Blood glucose levels at each nuclear magnetic resonance acquisition period. (CPB = *cardiopulmonary bypass.)*

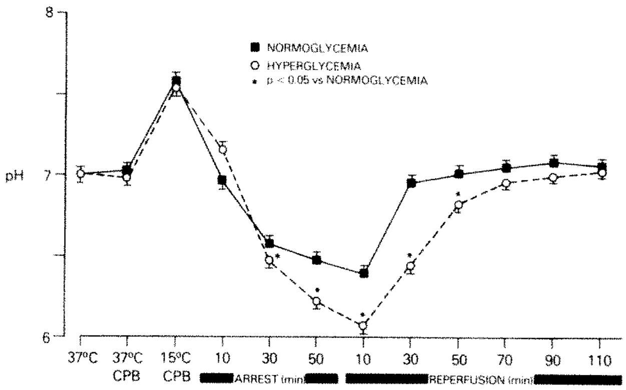


Fig 2. Cerebral intracellular pH. (CPB = *cardiopulmonary bypass.)*

chemical shift at 37°C and 15°C has been determined previously [6].

Statistical Analysis

All results are reported as the mean ± the standard deviation. Statistical significance to the 95% confidence level was determined using the Excel Statmac macro statistical program. Unpaired Student's *t* tests were used for intergroup comparisons of means. A multivariate two-factor (group, period) analysis of variance was used as an omnibus screening test, followed by univariate two-factor analyses of variance and post hoc *t* tests.

Results

Serum glucose levels were significantly greater in the hyperglycemic group throughout each acquisition period (Fig 1). Changes in ATP, PCr, and pH are shown in Table 1. Cardiopulmonary bypass at 15°C produced an increase in intracellular pH in control and hyperglycemic animals (Fig 2). This is consistent with the observations of our group [5, 7] using a similar model. During the arrest period and through the first 20 minutes of reperfusion, the intracellular pH markedly decreased in both groups. Compared with the normoglycemic group, the hyperglycemic animals became significantly more acidotic. Intracellular pH returned to baseline after 30 minutes of reperfusion in the normoglycemic group but did not reach baseline until 1 hour of reperfusion in the hyperglycemic animals.

The ATP and PCr concentrations followed a course similar to that of pH. Hypothermic bypass resulted in increased levels of ATP and PCr in both groups, which subsequently decreased with circulatory arrest. Compared with the normoglycemic animals, the hyperglycemic group demonstrated significantly higher concentrations of ATP during hypothermic bypass and arrest (Fig 3). Repletion of ATP during the reperfusion period was similar for both groups.

Table 1. Changes in High-Energy Phosphates and Intracellular pH[a]

	pH_i		%Δ PCr		%Δ ATP	
Time	NG	HG	NG	HG	NG	HG
37°C	7.01 ± 0.03	7.01 ± 0.02	100	100	100	100
37°C CPB	7.01 ± 0.02	6.99 ± 0.05	99 ± 3	95 ± 4	99 ± 5	98 ± 3
15°C CPB	7.59 ± 0.02	7.56 ± 0.06	123 ± 5	125 ± 6	109 ± 5	115 ± 5^{b}
Arrest (min)						
10	6.98 ± 0.26	7.17 ± 0.03	69 ± 10	78 ± 9	86 ± 4	107 ± 6^{c}
30	6.58 ± 0.06	6.48 ± 0.05^{d}	29 ± 5	30 ± 5	44 ± 4	62 ± 8^{c}
50	6.48 ± 0.05	6.23 ± 0.07^{c}	20 ± 4	20 ± 6	34 ± 5	40 ± 2^{d}
Reperfusion (min)						
10	6.40 ± 0.08	6.08 ± 0.06^{c}	60 ± 6	54 ± 7	67 ± 5	74 ± 7
30	6.97 ± 0.08	6.46 ± 0.23^{c}	109 ± 6	87 ± 13^{c}	92 ± 4	96 ± 6
50	7.03 ± 0.08	6.84 ± 0.18^{b}	110 ± 6	97 ± 10^{d}	93 ± 4	93 ± 4
70	7.07 ± 0.05	6.98 ± 0.15	113 ± 9	101 ± 15	90 ± 7	89 ± 6
90	7.11 ± 0.08	7.02 ± 0.14	112 ± 8	103 ± 13	89 ± 5	89 ± 6
110	7.07 ± 0.03	7.05 ± 0.14	112 ± 7	103 ± 14	90 ± 6	89 ± 8

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ compared with normoglycemic group. [c] Significance: $p < 0.001$ compared with normoglycemic group. [d] Significance: $p < 0.01$ compared with normoglycemic group.

ATP = adenosine triphosphate; CPB = cardiopulmonary bypass; HG = hyperglycemia; NG = normoglycemia; PCr = phosphocreatine; pH_i = intracellular pH.

Barbiturates Impair Cerebral Metabolism During Hypothermic Circulatory Arrest

Michael G. Siegman, MD, Richard V. Anderson, MD, Robert S. Balaban, PhD,
Toni L. Ceckler, PhD, Richard E. Clark, MD, and Julie A. Swain, MD

Surgery Branch and Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland; Cardiovascular and Pulmonary Research Center, Allegheny Singer Hospital, Pittsburgh, Pennsylvania; and Department of Surgery, University of Nevada School of Medicine, Las Vegas, Nevada

Barbiturates have been used as a method of cerebral protection in patients undergoing open heart operations. Phosphorus 31 nuclear magnetic resonance spectroscopy was used to assess barbiturate-induced alterations in the cerebral tissue energy state during cardiopulmonary bypass, hypothermic circulatory arrest, and subsequent reperfusion. Sheep were positioned in a 4.7-T magnet with a radiofrequency coil over the skull. Nuclear magnetic resonance spectra were obtained at 37°C, during cardiopulmonary bypass before and after drug administration at 37°C and 15°C, throughout a 1-hour period of hypothermic circulatory arrest, and during a 2-hour reperfusion period. A group of animals (n = 8) was administered a bolus of sodium thiopental (40 mg/kg) during bypass at 37°C followed by an infusion of 3.3 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until hypothermic arrest. A control group of animals (n = 8) received no barbiturate. The phosphocreatine/adenosine triphosphate ratio, reflecting tissue energy state, was lower during cardiopulmonary bypass at 15°C in the treated animals compared with controls (1.06 ± 0.08 versus 1.36 ± 0.17; $p < 0.001$). Lower phosphocreatine/adenosine triphosphate ratios were observed throughout all periods of arrest and reperfusion in the barbiturate-treated animals compared with controls ($p \leq 0.01$). Thiopental prevented the increase in cerebral energy state normally observed with hypothermia and resulted in a decrease in the energy state of the brain during hypothermic circulatory arrest and subsequent reperfusion. These results suggest that thiopental administration before a period of hypothermic circulatory arrest may prove detrimental to the preservation of the energy state of the brain.

(Ann Thorac Surg 1992;54:1131–6)

Barbiturates have been used as a method of cerebral protection to prevent ischemic injury. Barbiturates reduce both the size of ischemia-induced cerebral infarcts [1, 2] and the corresponding functional deficit in primates [1]. Clinical trials [3] have demonstrated that the neuropsychiatric complications of intracardiac operations can be lessened by barbiturate administration.

See also page 1126.

Phosphorus 31 nuclear magnetic resonance spectroscopy (NMR) enables accurate in vivo measurement of high-energy phosphate concentrations and intracellular pH [4]. Its use in the study of cerebral metabolism is well established [5–8]. The objective of this study was to determine the effect of a barbiturate on the cerebral tissue energy state when administered before an interval of hypothermic circulatory arrest.

Material and Methods

Animal Preparation

The experimental design used in this study was approved by the Animal Care and Use Committee of the National Heart, Lung, and Blood Institute in accordance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

Thirty-five hornless juvenile sheep greater than 8 weeks of age and weighing between 16 and 25 kg were used in this study. Sheep older than 8 weeks have no 2,3-diphosphoglycerate in the blood, and this allows a more accurate determination of the resonance position of inorganic phosphate for the calculation of intracellular pH. Animals were randomized to the treatment or control group.

Anesthesia was induced in all animals with intravenous administration of Telazol (10 mg/2.5 kg), a nonnarcotic, nonbarbiturate, injectable anesthetic agent that is a combination of equal parts by weight of base of liletamine hydrochloride and zolazepam hydrochloride. The animals were intubated and maintained on 99% oxygen/1% halothane inhalation anesthesia. Pancuronium bromide (0.1 mg/kg) was administered intravenously for muscle paralysis, and the animals were ventilated with a pediatric

---

Accepted for publication May 4, 1992.

Address reprint requests to Dr Swain, Division of Cardiovascular Surgery, University of Nevada School of Medicine, 2040 W Charleston Blvd, Suite 601, Las Vegas, NV 89102.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

volume ventilator (model D-900; Siemans-Allis, Cherry Hill, NJ).

Femoral artery pressure and venous infusion catheters were placed in all animals, and the skin and subcutaneous tissue over the frontal and parietal regions of the skull were removed using electrocautery for hemostasis. The animals were given heparin sodium (300 U/kg), after which either a 14F or 16F arterial cardiopulmonary bypass (CPB) cannula was placed in the left femoral artery and a 24F venous cannula was inserted into the right atrium through the right internal jugular vein. The animals were wrapped in an insulating blanket and placed in a cradle to facilitate subsequent positioning in the bore of the magnet. An insulated single-turn custom-made radiofrequency coil 2 cm in diameter was secured with tape over the skull.

Arterial pressure was measured using a Statham P23 pressure transducer (Spectramed Inc, Oxnard, CA) connected to a strip-chart recorder. Mean arterial pressure was maintained between 60 and 90 mm Hg at 37°C and 30 to 60 mm Hg at 15°C. Arterial blood gases were measured intermittently using a Radiometer model ABL 300 blood gas analyzer (Radiometer America, Westlake, OH). Arterial oxygen tension was maintained greater than 100 mm Hg, and carbon dioxide tension ranged from 25 to 45 mm Hg during CPB. Alpha-stat pH management was employed during hypothermia.

Cardiopulmonary Bypass

The CPB circuit consisted of a centrifugal pump (model BP-80; Bio-Medicus, Eden Prairie, MN), a 33-μm arterial filter (model H-625; Bard Cardiopulmonary Division, Santa Ana, CA), and a hollow-fiber membrane oxygenator with integral heat exchanger (Maxima; Medtronic Blood Systems, Inc, Anaheim, CA). A cardiotomy reservoir (Gish Biomedical, Inc, Santa Ana, CA) was placed in the venous side of the circuit to permit the rapid administration of fluid during CPB as well as the exsanguination of the animal during circulatory arrest.

During hypothermic circulatory arrest, the blood was recirculated at low flow to minimize blood damage. The temperature of the recirculating blood was maintained at 15°C. The centrifugal pump and the electromagnetic flowmeter remained 4.5 m from the magnet where they have been shown to perform normally in the approximately 15-G magnetic field present at this distance. The circuit was primed with 2,500 mL of lactated Ringer's solution, 400 mL of homologous whole blood, 10,000 units of heparin, 50 mEq of sodium bicarbonate, and 12.5 g of mannitol.

Blood flows were maintained between 60 and 100 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ during CPB. During cooling, nasopharyngeal temperature was measured with a nonmagnetic, thermistor-tipped temperature probe connected to a Gould temperature amplifier (model 13-4615-474029; Gould Inc, Recording System Division, Cleveland, OH).

Nuclear Magnetic Resonance Spectroscopy

The animals were positioned so that the brain was centered in an Oxford Instruments 4.7-T 40-cm-bore magnet (Oxford, England). The surface coil was tuned to 81 MHz and matched to 50 Ω. The magnet was interfaced with a General Electric CSI spectrometer (General Electric NMR Instruments, Fremont, CA). Homogeneity of the magnetic field was determined using the proton free induction decay at 200 MHz. Phosphorus 31 NMR spectra were collected with a 2-second interpulse delay in 64 acquisition (2-minute) blocks. The pulse width was adjusted to maximize the signal from the cerebral cortex based on the phosphocreatine (PCr) signal. The signal from bone was minimized with a 2-second preirradiation saturation pulse at 13.05 ppm from PCr using a homonuclear decoupler [9]. Every ten sequential spectra (20 minutes) were block-averaged before data analysis. The spectra were analyzed using the GEMCAP Lorentzian line-fitting program, resident in the General Electric software.

Thiopental Dose

Determination of the dose of sodium thiopental to be administered was based on results of studies performed on a group of sheep (n = 4) similar to that used in the experimental protocol. The NMR apparatus did not permit accurate monitoring of the electroencephalogram while the animals were in the magnet, thereby necessitating the determination of a standard dose of thiopental before the actual experiments. Silver electroencephalographic leads were placed at the level of the posterior table of the skull over the parietal area. The animals were placed on CPB at 37°C after which thiopental was administered in 250-mg boluses every 2 to 3 minutes until there was cessation of electrocortical activity as determined by electroencephalography. Once cessation of electrocortical activity was obtained, continuous infusion of thiopental was begun (50 mg/mL) and the rate adjusted to maintain an isoelectric electroencephalogram with a burst suppression pattern with more than 60 seconds between bursts. This was continued while the animal was cooled to 15°C (an interval of 30 to 60 minutes). The highest loading dose required was 36 mg/kg, and the maintenance doses required averaged between 2.8 and 3.3 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

Therefore, it was decided to administer a loading dose of 40 mg/kg and a maintenance dose of 3.3 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ to each sheep in this nonsurvival study to ensure adequate suppression of electrocortical activity. The mean dose used in this experiment was 346 mg/kg. The mean dose used by Nussmeier and associates [3] in a study investigating barbiturate use in humans during normothermic CPB was 40 ± 8 mg/kg.

Experimental Protocol

Initial NMR spectra were acquired for all animals at 37°C. The animals were placed on CPB, and NMR spectra were again acquired once hemodynamic stability had been achieved. A bolus of sodium thiopental (40 mg/kg) was then administered to the treatment group (n = 23) over a 5-minute period and was followed by an infusion of 3.3 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until hypothermic circulatory arrest. The control animals (n = 12) received an identical vehicle without barbiturate. Nuclear magnetic resonance spectra were obtained during this steady-state barbiturate administration. Dopamine hydrochloride (6 to 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was initiated in the barbiturate-treated animals 10 minutes before the administration of sodium thiopental to preserve systemic blood pressure and ensure an adequate cerebral perfusion pressure. Halothane anesthesia was discontinued in the treated animals once the thiopental bolus was begun.

All animals were then cooled to a nasopharyngeal temperature of 15°C over an interval of 30 to 60 minutes. This was followed by a 1-hour period of circulatory arrest (during which halothane administration was discontinued) and a 2-hour reperfusion and rewarming period. The NMR spectra were acquired in both groups of animals on CPB at 15°C and throughout the entire period of circulatory arrest and reperfusion. Before reperfusion, 80 mg of lidocaine hydrochloride, 25 g of mannitol, and a second unit (400 mL) of homologous whole blood was added to the cardiotomy reservoir. Inotropic support (5 to 12 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine) was initiated with reperfusion in all animals. The animals were rewarmed over 30 minutes by maintaining a 10°C gradient between blood and water bath temperatures. Halothane 1% was given to all animals during reperfusion. Animals able to maintain stable arterial pressures greater than 50 mm Hg were weaned from CPB (1/8 treated animals and 5/8 control animals). At the completion of the 2-hour reperfusion period, animals were killed with intravenous administration of potassium chloride.

Animals were excluded from the study for any of the following reasons: (1) signs of massive fluid overload with pink, frothy fluid in the ventilator tubing, (2) inability to maintain adequate blood flow on CPB because of technical difficulties, and (3) failure to exhibit return of cerebral adenosine triphosphate (ATP) concentration on reperfusion, indicating failure to adequately reperfuse the brain. Fifteen animals in the treated group and 4 controls were excluded.

Data Analysis

The relative concentrations of ATP and PCr compared with baseline values obtained at 37°C before bypass were calculated from the NMR spectra. The resonance frequency of inorganic phosphate was used to determine intracellular pH. A factor of 1.5, used to correct the PCr/ATP ratio for the spin-lattice relaxation time at the 2-second acquisition repetition rate (the T1 correction factor) [7], was not employed, as our experiment yielded relative concentrations only.

Results were expressed as the mean ± the standard deviation. Statistical significance (to the 95% confidence level) was determined with the Statmac statistical program (developed by Dan Moore; IBM conversion by Heizer Software, Pleasant Hill, CA). The unpaired Student's t test was used for intergroup comparisons between the control and barbiturate-treated animals at 37°C, during normothermic (37°C) and hypothermic (15°C) CPB, during hypothermic circulatory arrest, and throughout the rewarming and reperfusion period.

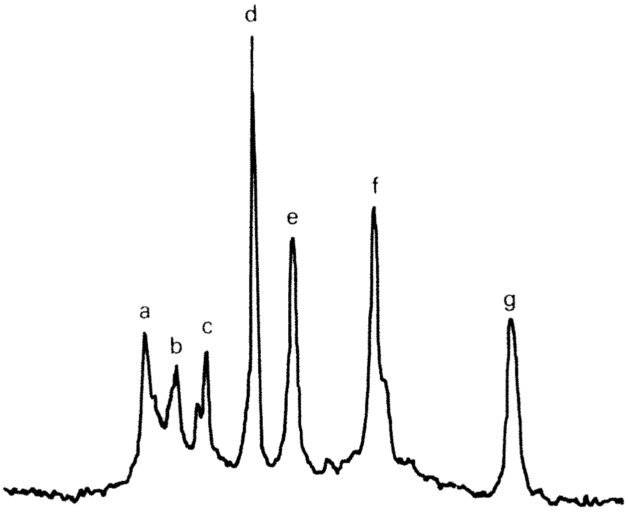


Fig 1. Typical phosphorus 31 nuclear magnetic resonance spectrum from sheep brain at 37°C before cardiopulmonary bypass. The spectrum represents 640 acquisitions over 20 minutes. Ten-hertz exponential line broadening was applied before Fourier transformation. Peak assignments are: (a) phosphomonoesters, (b) inorganic phosphate, (c) phosphodiesters, (d) phosphocreatine, (e) γ-adenosine triphosphate (ATP), (f) α-ATP, and (g) β-ATP.

Results

A typical NMR spectrum obtained from a control animal at 37°C before CPB is shown in Figure 1. Hemoglobin, arterial oxygen content, carbon dioxide tension, arterial pH, arterial blood pressure, and pump flow were measured during the various periods of the experiment (excluding the arrest period). Attempts were made to keep these variables steady during each interval. There were no major differences between control and experimental groups in the values for these variables for each interval. Serum osmolarity was not measured in either control or barbiturate-treated animals. The ATP and PCr concentrations, reported as percent change from baseline values obtained at 37°C before CPB, are shown in Table 1. The PCr/ATP ratio for both groups is shown in Figure 2.

The barbiturate-treated animals showed significantly lower levels of PCr after the administration of thiopental during CPB at both 37°C and 15°C before hypothermic circulatory arrest ($p < 0.05$). Thiopental administration maintained a higher level of ATP during hypothermic circulatory arrest in the treated animals, with ATP preserved at 41% of prearrest value after 60 minutes of arrest compared with 33% for control animals ($p < 0.01$). The PCr levels were significantly lower in the treated animals compared with controls during this period ($p < 0.05$) as well as during the final 100 minutes of reperfusion ($p < 0.005$).

The administration of sodium thiopental was associated with lower PCr/ATP ratios than in the control animals during CPB at both 37°C and 15°C ($p < 0.05$). During arrest and reperfusion, relatively parallel rates of change in the PCr/ATP ratio were demonstrated, although the ratio was lower throughout these periods in the treated animals ($p \leq 0.01$).

Table 1. Effect of Barbiturate Administration Before Hypothermic Circulatory Arrest[a]

	%ΔPCr		%ΔATP		PCr/ATP Ratio	
Time	Control	Barbiturate	Control	Barbiturate	Control	Barbiturate
37°C	100	100	100	100	1.03 ± 0.16	0.96 ± 0.16
(Barbiturate administration begun)						
CPB						
37°C	104 ± 11	94 ± 7[b]	99 ± 8	96 ± 6	1.07 ± 0.11	0.93 ± 0.09[b]
15°C	121 ± 15	104 ± 16[b]	90 ± 9	93 ± 10	1.36 ± 0.17	1.06 ± 0.08[b]
Arrest (min)						
10	72 ± 12	64 ± 12	75 ± 10	83 ± 10	0.98 ± 0.10	0.73 ± 0.10[b]
30	30 ± 3	28 ± 6[b]	41 ± 5	55 ± 8[b]	0.74 ± 0.09	0.48 ± 0.09[b]
50	21 ± 6	14 ± 3[b]	33 ± 5	41 ± 5[b]	0.67 ± 0.20	0.33 ± 0.09[b]
Reperfusion (min)						
10	62 ± 10	63 ± 11	63 ± 6	75 ± 10[b]	0.99 ± 0.1	0.79 ± 0.08[b]
30	114 ± 17	92 ± 13[b]	88 ± 10	91 ± 8	1.32 ± 0.15	0.97 ± 0.13[b]
50	115 ± 8	87 ± 14[b]	88 ± 8	86 ± 7	1.34 ± 0.16	0.97 ± 0.18[b]
70	112 ± 14	88 ± 14[b]	89 ± 12	84 ± 8	1.27 ± 0.15	1.03 ± 0.18[b]
90	116 ± 15	91 ± 17[b]	89 ± 6	83 ± 9	1.32 ± 0.19	1.05 ± 0.15[b]
110	113 ± 11	89 ± 17[b]	88 ± 6	85 ± 9	1.31 ± 0.15	1.00 ± 0.16[b]

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ compared with control group.

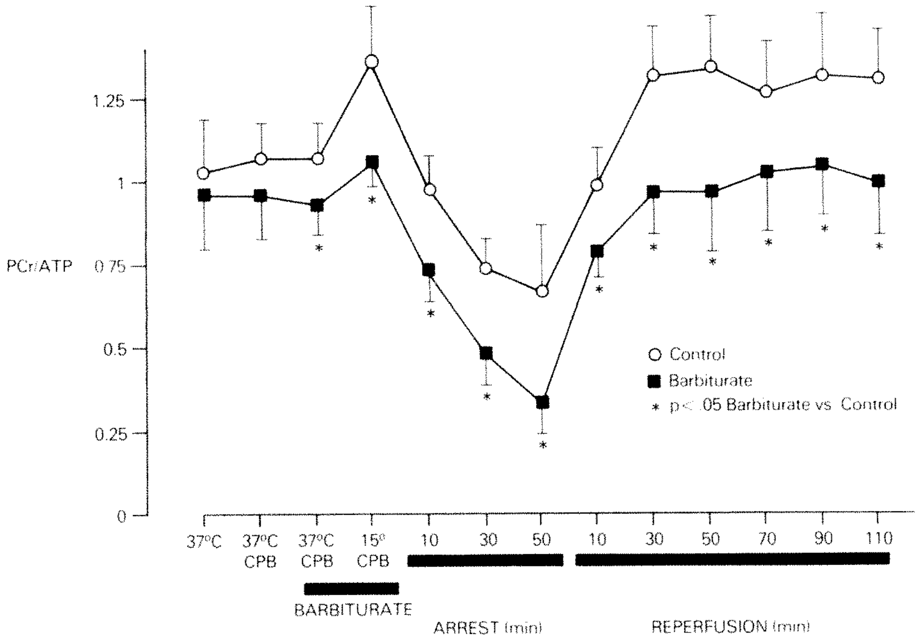
ATP = adenosine triphosphate; CPB = cardiopulmonary bypass; PCr = phosphocreatine.

Several overlapping peaks at the resonance frequency of inorganic phosphate were observed after the administration of thiopental (Fig 3), preventing a single determination of intracellular pH, which is derived from the spectral shift of inorganic phosphate from PCr. Such a range of resonance positions in the barbiturate-treated animals was thought to be due to a distribution of intracellular pH values. This pH distribution will be discussed further in our comment.

Comment

Debilitating cerebral complications continue to occur after cardiac operations despite improvements in both operative technique and CPB apparatus. Systemic hypothermia is the primary form of cerebral protection used during CPB. Deep hypothermia is employed as a means of cerebral protection during procedures requiring total circulatory arrest including the repair of congenital cardiac defects and aortic arch aneurysms as well as resection of tumors near or at the base of the brain. Deep hypothermia in this setting extends the limited "safe" period of total circulatory arrest. One beneficial effect of hypothermia is a reduction in cerebral metabolic demand. Additional protective effects of hypothermia have been found by our group [8] using phosphorus 31 NMR spectroscopy to demonstrate that hypothermia increases the energy state and intracellular pH in the brain.

Fig 2. Changes in the phosphocreatine/adenosine triphosphate (PCr/ATP) ratio for both the barbiturate-treated animals and controls at selected periods throughout the course of the experiment.



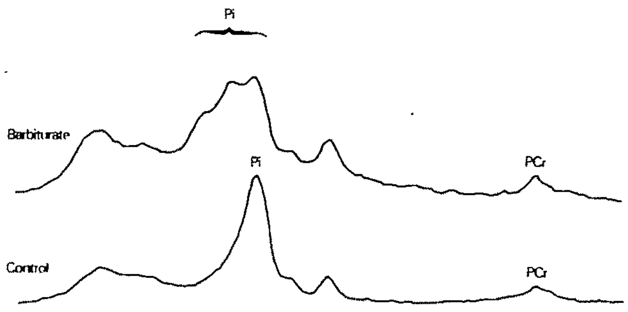


Fig 3. Spectra obtained from a barbiturate-treated animal and a control animal during the interval of 20 to 40 minutes of hypothermic circulatory arrest. Note the overlapping peaks at the resonance frequency of inorganic phosphate (Pi) in the barbiturate-treated animal. The spectra are aligned at the peak representing phosphocreatine (PCr) to accurately demonstrate the spectral shift of Pi in the treated animals to a range of frequencies representing more alkaline intracellular pH values, ie, a leftward shift. These spectra represent 640 acquisitions over 20 minutes.

Alternate methods of cerebral protection have been sought for many years. Much of the work in this area has centered on the study of various pharmacologic agents. Four major approaches to pharmacologic intervention to reduce cerebral injury during cardiac operations include reducing cerebral metabolism, reducing free radical and reperfusion injury, preventing microemboli with antiplatelet and antineutrophil agents, and reducing intracellular calcium increases [10].

Barbiturates represent one of the earliest and most extensively studied agents. Sodium pentobarbital was shown to decrease lactate accumulation and improve maintenance of ATP and PCr levels in primates when used to induce and maintain anesthesia before normothermic cerebral ischemia via middle cerebral artery occlusion compared with animals receiving halothane anesthesia [1]. Survival, degree of neurological deficit, and size of infarction were all significantly better in animals anesthetized with pentobarbital. Additional studies [2] have confirmed the protective effects of barbiturate administration against normothermic regional ischemic injury in primates.

The combined use of pentobarbital anesthesia and moderate hypothermia was found to decrease cerebral metabolism in dogs to a greater degree than achieved with either hypothermia or barbiturate alone [11, 12]. The use of a barbiturate as an adjunct to hypothermia to obtain a greater cerebroprotective effect was investigated in a prospective, randomized clinical trial by Nussmeier and colleagues [3]. Their study demonstrated the efficacy of thiopental, administered in a sufficient dose before the initiation of hypothermic CPB, to reduce the neuropsychiatric complications of intracardiac operations requiring CPB. This was the first demonstration of cerebral protection by a barbiturate in humans.

The results of the present study do not support the use of thiopental as an adjunct to hypothermic cerebral protection during open heart procedures. The administration of thiopental prevented the increase in cerebral energy state normally observed with hypothermia [8] and resulted in a decrease in the energy state of the brain, as determined by the PCr/ATP ratio, during hypothermic circulatory arrest and subsequent reperfusion. Although the ATP level was maintained slightly higher during hypothermic circulatory arrest in the barbiturate-treated animals compared with controls, PCr concentration and overall free energy were reduced. This discrepancy could be due to an inhibition of adenylate kinase activity, which would prevent the breakdown of adenosine diphosphate to adenosine monophosphate and serve to maintain higher adenosine diphosphate and ATP levels. However, there is no evidence for such a mechanism in the present study.

The range of intracellular pH values during hypothermic circulatory arrest and early reperfusion in each barbiturate-treated animal was found to be more alkaline compared with the single pH value of the control animals obtained during the same intervals (see Fig 3). Throughout the final 40 minutes of hypothermic circulatory arrest, the range of pH values in the treated group was 6.4 to 7.2 compared with a mean intracellular pH of 6.5 ± 0.1 in the control group.

The finding of a range of more alkaline pH values in the barbiturate-treated animals during hypothermic circulatory arrest implies a regional inhibition of lactic acid production from glycolysis. The decrease in ATP production by glycolysis could result in the buildup of adenosine diphosphate, which, in turn, could cause a marked fall in PCr levels. This would result in a decrease in the PCr/ATP ratio, reflective of the lowered energy state of the brain. Investigation into the metabolic mechanisms of barbiturate action may help elucidate the spectroscopic findings demonstrated and help explain the pH and energy metabolism alterations observed.

As stated in the experimental protocol, dopamine was given to the barbiturate-treated animals immediately before thiopental administration to counter the hemodynamic effects of the barbiturate and maintain an adequate cerebral perfusion pressure while on CPB. We must recognize the possibility that dopamine may have played a role in the decreased energy state of the barbiturate-treated animals. In consideration of this possibility, several points should be recognized. First, it is known that although there are specific dopaminergic receptors in the central nervous system, injected dopamine usually has no central effects because it does not normally cross the blood-brain barrier, although no data relating to the blood-brain barrier concerning dopamine during CPB are available. Second, the decreased energy state in the barbiturate-treated animals was observed throughout circulatory arrest and reperfusion despite dopamine administration to both groups of animals. Finally, the provision of cardiovascular support with inotropic and α-adrenergic agents corresponds to the clinical situation during barbiturate administration.

Although conclusive functional correlation is not available, these results suggest that barbiturate administration before a period of hypothermic circulatory arrest is not cerebroprotective and may prove detrimental to the preservation of the energy state of the brain possibly by inhibiting glycolysis. Barbiturate administration to patients undergoing operative procedures associated with cerebral ischemia, particularly those involving systemic hypothermia, warrants reevaluation and further study.

We thank Stephanie Sellers, BA, for technical assistance.

References

1. Michenfelder JD, Milde JH. Influence of anesthetics on metabolic, functional and pathological responses to regional cerebral ischemia. Stroke 1975;6:405–10.
2. Hoff JT, Smith AL, Hankinson HL, Nielson SL. Barbiturate protection from cerebral infarction in primates. Stroke 1975; 6:28–33.
3. Nussmeier NA, Arlund C, Slogoff S. Neuropsychiatric complications after cardiopulmonary bypass: cerebral protection by a barbiturate. Anesthesiology 1986;64:165–70.
4. Balaban RS. NMR spectroscopy of the heart, part 1. Concepts Magn Reson 1989;1:15–26.
5. Stocker F, Herschkowitz N, Bossi E, et al. Cerebral metabolic studies in situ by 31-P nuclear magnetic resonance after hypothermic circulatory arrest. Pediatr Res 1986;20:867–71.
6. Norwood WI, Norwood CR, Ingwall JS, Castaneda AR, Fossel ET. Hypothermic circulatory arrest: 31-phosphorus nuclear magnetic resonance of isolated perfused neonatal rat brain. J Thorac Cardiovasc Surg 1979;78:823–30.
7. Swain JA, Robbins RC, Balaban RS, McDonald TJ, Schneider B, Groom RC. The effect of cardiopulmonary bypass on brain and heart metabolism: a 31-P NMR study. Magn Reson Med 1990;15:446–55.
8. Swain JA, McDonald TJ Jr, Balaban RS, Robbins RC. Metabolism of the heart and brain during hypothermic cardiopulmonary bypass. Ann Thorac Surg 1991;51:105–9.
9. Ackerman JJH, Evelhoch JL, Berkowitz BA, Kichura GM. Selective suppression of the cranial bone resonance from ^{31}P NMR experiments with rat brain in vivo. J Magn Reson 1984;56:318–22.
10. Royston D. Interventions to reduce cerebral injury during cardiac surgery: the effect of physical and pharmacological agents. Perfusion 1989;4:153–61.
11. Lafferty JJ, Keykhah MM, Shapiro HM, Van Horn K, Behar MG. Cerebral hypometabolism obtained with deep pentobarbital anesthesia and hypothermia (30°C). Anesthesiology 1978;49:159–64.
12. Steen PA, Newberg L, Milde JH, Michenfelder JD. Hypothermia and barbiturates: individual and combined effects on canine cerebral oxygen consumption. Anesthesiology 1983; 58:527–32.

Coronary Sinus Injuries During Retrograde Continuous Normothermic Blood Cardioplegia

Anthony L. Panos, MD, Imtiaz S. Ali, MD, Peter L. Birnbaum, MD,
Carlos A. M. Barrozo, MD, Owayed Al-Nowaiser, MD, and Tomas A. Salerno, MD

Division of Cardiovascular Surgery, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

Injuries to the coronary sinus during cardioplegic arrest are rare but potentially lethal. We herein present case reports of injuries to the coronary sinus occurring during retrograde continuous normothermic blood cardioplegia, and emphasize preventive measures and treatment.

(Ann Thorac Surg 1992;54:1137–8)

Over the past 10 years there has been a resurgence in the technique of retrograde coronary sinus (CS) cardioplegia [1]. The CS has been used as a route of delivery in several myocardial protective techniques including intermittent cold crystalloid [2, 3] and intermittent cold blood cardioplegia [4]. Recently, our group at the University of Toronto has introduced the technique of retrograde continuous normothermic blood cardioplegia (RCNBC) [5]. Despite widespread use of retrograde CS cardioplegia [6], little has been reported regarding CS injuries [2]. This article describes detailed case reports of CS injuries during RCNBC, emphasizing preventive measures, techniques of surgical repair, and alternative methods of cardioplegia administration.

Case Reports

Case 1: High Coronary Sinus Pressure and Rupture

A 56-year-old man underwent coronary artery bypass grafting for severe three-vessel coronary artery disease and had a grade IV ventricle. At operation and during cardioplegic arrest using the Normoplegia coronary sinus cannula (Research Medical Inc, Salt Lake City, UT), problems occurred in the pump head of the cardioplegia delivery system. In the process of attempting to correct the problem, the CS was exposed to pressures in excess of 180 mm Hg for a brief period, as the pressurized and clamped lines were inadvertently unclamped. Upon resumption of cardioplegia, the perfusion pressure was very low (4 mm Hg) and arterialized blood was observed to be coming from the posterior surface of the heart. On inspection, total rupture of the CS was noted. The cardioplegic infusion was immediately discontinued and was resumed in an antegrade (normothermic cardioplegia) fashion. Before aortic unclamping, a large homologous pericardial patch was used to cover the shredded edges of the CS and the hematoma that had developed. Weaning from bypass was uneventful, and the patient had a smooth postoperative course and was discharged home on the 8th postoperative day.

Case 2: Perforation of the Coronary Sinus by Normoplegia Catheter

A 65-year-old man underwent coronary artery bypass grafting using RCNBC. During construction of the distal anastomoses and while the heart was retracted, low perfusion pressures occurred (<6 mm Hg), suggesting displacement of the CS catheter. An attempt was made to reinsert the CS catheter, resulting in perforation of the CS in its midportion. The injury was immediately recognized and direct repair was carried out with a 6-0 Prolene suture (Ethicon, Somerville, NJ). The operation was completed using antegrade continuous normothermic blood cardioplegia, and the patient recovered uneventfully.

Cases 3 and 4: Hematoma of the Distal Coronary Sinus

One patient underwent coronary artery bypass grafting and the other patient underwent mitral valve replacement. At operation, high pressures (>80 mm Hg) were noted in the CS, leading to immediate discontinuation of cardioplegia delivery. Inspection revealed a large hematoma in the distal portion of the CS without obvious perforation. Retrograde continuous normothermic blood cardioplegia was discontinued, and antegrade normothermic blood cardioplegia was instituted. The hematoma was left untreated. The patients had uneventful postoperative recoveries.

Case 5: Perforation of the Right Ventricle

During RCNBC in a patient undergoing a coronary artery operation, the pressures in the CS infusion suddenly decreased from 32 to 6 mm Hg, indicating displacement of the CS cannula. In an attempt to reposition the CS catheter with its stylette in place, perforation of the flaccid right ventricle occurred. This was repaired with pledgeted 3-0 Prolene sutures. The operation was completed successfully using antegrade continuous normothermic blood cardioplegia.

Comment

Injury of the CS is a potential complication of all myocardial protective techniques requiring cannulation of the CS. Menasché and associates [2] have reported a 0.6% incidence of CS injury in a series of 500 patients receiving

Accepted for publication March 27, 1992.

Address reprint requests to Dr Salerno, St. Michael's Hospital, Rm 305B, 30 Bond St, Toronto, Ont, Canada M5B 1W8.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

cold intermittent crystalloid cardioplegia through the CS during aortic valve operations. This compares favorably with the 1% to 5% incidence of complications due to ostial cannulation during antegrade cardioplegia [6]. The present report describes traumatic injuries of the CS during RCNBC. We were concerned that the requirement of continuous delivery of blood cardioplegia during RCNBC might result in more manipulation of the CS catheter during the operation and might lead to more CS injuries. Therefore, it appears that injury to the CS is a feature of the technique of CS cannulation, and not continuous normothermic blood cardioplegia itself.

The key to avoiding CS injury during delivery of retrograde cardioplegia is careful and gentle placement of the catheter as described previously [7]. As illustrated by cases 2 and 5, extreme caution and gentle maneuvering of the CS catheter is required when the stylette is in place, as maneuvering may cause perforation of the CS or right ventricle. Repositioning of the CS catheter during cardioplegic arrest may be difficult, as the CS is empty of blood and is usually collapsed. If the catheter is dislodged from the CS we have usually been able to reinsert the catheter by gentle manipulation. However, if the catheter cannot be easily reinserted into the CS, then one can either open the right atrium and insert it under direct vision (possible in cases where double venous cannulation has been used) or else change to the antegrade method of cardioplegia delivery.

As reflected by cases 1, 3, and 4, exposure of the CS to pressures in excess of those recommended, ie, 40 to 50 mm Hg [8], is unwise and dangerous. The sequelae of such precipitous increases in CS pressure are hematoma formation and CS rupture. In general, the hematoma can be left untreated with no deleterious consequences. However, rupture of the CS must be addressed, and in our patient was successfully repaired by suturing of a homologous pericardial patch over the shredded edges of the CS.

Upon recognition of any problem with RCNBC, the surgeon should attempt to understand the problem and take the necessary measures to correct it. Alternatively, it may be necessary to immediately switch to other methods of myocardial protection, such as antegrade cardioplegic techniques (normothermic or hypothermic).

When they occur and are recognized, CS injuries can be effectively treated and, to date, have not resulted in serious sequelae. Potentially, however, these injuries can be life-threatening.

In summary, serious injuries to the CS or the heart appear to be rare during RCNBC. Usually they occur during insertion or manipulation of the CS catheter during RCNBC, particulary after arrest of the heart. It would appear that the majority of these injuries can be prevented. Although in some cases the cause remains unknown, it is certain that they are traumatic in nature. Recognition and correction of the problem or the use of an alternative method of myocardial protection is indicated in these circumstances. When injuries occur and are recognized, they can be dealt with effectively. It is possible that unrecognized and clinically insignificant CS injuries could still occur in patients receiving RCNBC. Future detailed anatomical studies might clarify these observations.

Supported by grant MA-8044 from the Medical Research Council of Canada.

References

1. Menasche P, Piwnica A. Cardioplegia by way of the coronary sinus for valvular and coronary surgery. J Am Coll Cardiol 1991;18:628–36.
2. Menasché P, Subayi J-B, Piwnica A. Retrograde coronary sinus cardioplegia for aortic valve operations: a clinical report on 500 patients. Ann Thorac Surg 1990;49:556–64.
3. Guiraudon GM, Campbell CS, McLellan DG, et al. Retrograde coronary sinus versus aortic root perfusion with cold cardioplegia: randomized study of levels of cardiac enzymes in 40 patients. Circulation 1986;74(Suppl 3):105–15.
4. Buckberg GD. Antegrade/retrograde blood cardioplegia to ensure cardioplegic distribution: operative techniques and objectives. J Cardiac Surg 1989;4:216–38.
5. Salerno TA, Houck JP, Barrozo CAM, et al. Retrograde continuous warm blood cardioplegia: a new concept in myocardial protection. Ann Thorac Surg 1991;51:245–7.
6. Chitwood WR. Myocardial protection by retrograde cardioplegia: coronary sinus and right atrial methods. In: Cardiac surgery: state of the art reviews; vol 2. Philadelphia: Hanley and Belfus, 1988:197–218.
7. Salerno TA, Christakis GT, Abel J, et al. Technique and pitfalls of retrograde continuous warm blood cardioplegia. Ann Thorac Surg 1991;51:1023–5.
8. Menasché P, Kural S, Fauchet M, et al. Retrograde coronary sinus perfusion: a safe alternative for ensuring cardioplegic delivery in aortic valve surgery. Ann Thorac Surg 1982;34:647–58.

obtained with intravenous administration of pancuronium bromide, 0.1 mg/kg. Arterial pressure and venous infusion catheters were placed in the right femoral artery and vein, respectively. The left femoral artery was cannulated with a 14F or 16F CPB catheter. A 24F lighthouse-tip CPB cannula was placed into the right atrium through the right internal jugular vein. Heparin sodium (300 U/kg) was administered intravenously before arterial and venous cannulation. An insulated, single-turn, custom-made radiofrequency coil 2 cm in diameter was secured over the exposed skull. The animal was then wrapped in an insulating blanket, placed in a Lucite cradle, and positioned in a 4.7-T, 30-cm clear-bore magnet.

Arterial blood oxygen tension was maintained greater than 100 mm Hg; normothermic carbon dioxide tension was maintained between 35 and 45 mm Hg. Mean arterial pressure was maintained between 60 and 90 mm Hg at 37°C and between 40 and 60 mm Hg at 15°C. Nasopharyngeal temperature was monitored with a temperature probe unaffected by the magnetic field. Serum electrolyte and glucose levels were intermittently measured using a Chem Pro 1000 Clinical Chemistry Analyzer (Ortho Diagnostic Systems Inc, Raritan, NJ).

Cardiopulmonary Bypass

The bypass circuit consisted of a centrifugal pump (model BP-80; Bio-Medicus, Eden Prairie, MN), a 33-μm arterial filter (model H-625; Bard Cardiopulmonary Division, Santa Ana, CA), and a hollow-fiber membrane oxygenator with integral heat exchanger (Maxima; Medtronic Blood Systems, Inc, Anaheim, CA). A cardiotomy reservoir (Gish Biomedical, Inc, Santa Ana, CA) was inserted parallel to the venous line for the administration of volume and as a reservoir for exsanguination of the animal during the arrest period. The pump was positioned 4.5 m from the magnet, and this necessitated corresponding lengths of extension tubing. The pump was primed with 2,500 mL of lactated Ringer's solution, 10,000 units of heparin, 50 mEq of sodium bicarbonate, 12.5 g of mannitol, 80 mg of 2% lidocaine hydrochloride, and 1 unit of sheep whole blood.

Blood flow during CPB was maintained between 60 and 100 mL $\cdot$ kg^{-1} $\cdot$ min^{-1}. Flow was measured with an electromagnetic flowmeter (Bio-Medicus) that had previously been calibrated in the weak magnetic field (15 G) where the pump was positioned. The oxygenator was ventilated with a mixture of 1% halothane and 99% oxygen.

After baseline NMR spectra were acquired at 37°C for 20 minutes, the animal was cooled to 15°C. Cooling took 29 to 53 minutes. During hypothermia, the arterial blood pH was managed using the alpha-stat scheme. After spectra acquisition at 15°C for 20 minutes, circulation was arrested for 1 hour, followed by 2 hours of reperfusion and rewarming. Before reperfusion, 25 g of mannitol and a second unit of whole blood were added to the cardiotomy reservoir. Inotropic support (dopamine hydrochloride, 5 μg $\cdot$ kg^{-1} $\cdot$ min^{-1}) was initiated with reperfusion in all animals. Rewarming was accomplished by maintaining a 10°C gradient between the blood and water bath temperatures. Sheep in which massive edema developed, manifested as pulmonary edema in the ventilator tubing and no return of cerebral adenosine triphosphate (ATP) levels, were unable to be weaned from bypass and were excluded from the study. Four of the 12 control animals had to be excluded for this reason. (These 4 animals required large volumes of fluid to maintain adequate flows while on CPB.) None of the hyperglycemic animals showed massive edema. Animals weaned from bypass were ventilated for the duration of the experiment. No attempt was made to wean from the ventilator. At the completion of 2 hours of reperfusion, animals were killed with intravenous administration of potassium chloride. Total time on CPB, including the arrest period, ranged from 4 hours 20 minutes to 4 hours 48 minutes.

Glucose Monitoring and Treatment

All animals fasted 12 hours before the experiment. The initial glucose level was determined as soon as venous access was obtained but before the start of maintenance fluid administration. All animals were initially normoglycemic (glucose level < 8.3 mmol/L [150 mg/dL]). The control (normoglycemic) animals received lactated Ringer's as maintenance fluid. The animals in the hyperglycemic group were administered lactated Ringer's with 5% dextrose as maintenance fluid. By the time the animals were transferred to the magnet and preparations for CPB had been completed, the animals in the treatment group had become hyperglycemic (glucose level > 13.9 mmol/L [250 mg/dL]).

Serum glucose levels were measured before initiation of CPB, during CPB at 37°C, during CPB at 15°C, during early reperfusion, and at 1 hour of reperfusion when rewarming was complete. Animals in the treatment group with glucose levels that fell to less than 13.9 mmol/L received intravenous injections of 50% dextrose in 12.5-mEq increments until the level was once again greater than 13.9 mmol/L. This was necessary on only three occasions.

NMR Spectroscopy

The techniques of NMR spectroscopy used in this study have been described previously [5]. The animal was positioned so that the brain was centered in the bore of the magnet. The NMR data were collected with a General Electric CSI spectrometer (General Electric NMR Instruments, Fremont, CA). The data were acquired in 20-minute blocks of 640 averaged acquisitions at 37°C before CPB, 37°C on CPB, and 15°C on CPB. Nine consecutive 20-minute blocks were then acquired, three during the arrest period and six during the reperfusion and rewarming period. Data were analyzed using the GEMCAP Lorentzian line-fitting program, a part of the GEMCSI software.

Concentrations of ATP and phosphocreatine (PCr) are reported as percent change from baseline levels acquired at 37°C off CPB. Intracellular pH was determined by measuring the chemical shift of the inorganic phosphate peak relative to the position of the pH-independent PCr peak. The relation between pH and inorganic phosphate

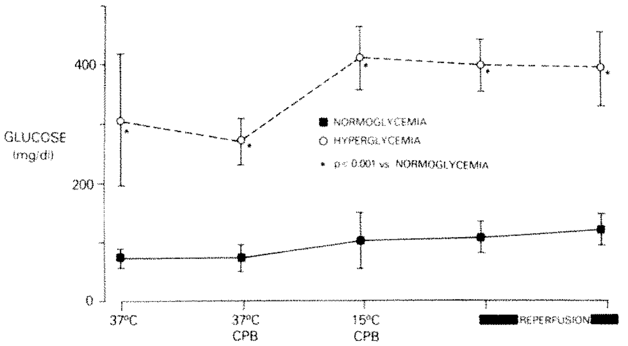


Fig 1. Blood glucose levels at each nuclear magnetic resonance acquisition period. (CPB = *cardiopulmonary bypass.)*

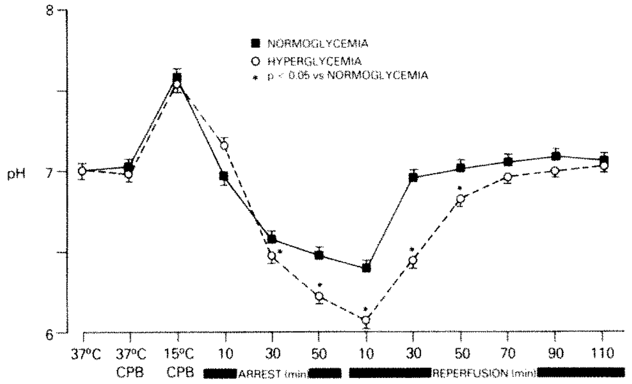


Fig 2. Cerebral intracellular pH. (CPB = *cardiopulmonary bypass.)*

chemical shift at 37°C and 15°C has been determined previously [6].

Statistical Analysis

All results are reported as the mean ± the standard deviation. Statistical significance to the 95% confidence level was determined using the Excel Statmac macro statistical program. Unpaired Student's *t* tests were used for intergroup comparisons of means. A multivariate two-factor (group, period) analysis of variance was used as an omnibus screening test, followed by univariate two-factor analyses of variance and post hoc *t* tests.

Results

Serum glucose levels were significantly greater in the hyperglycemic group throughout each acquisition period (Fig 1). Changes in ATP, PCr, and pH are shown in Table 1. Cardiopulmonary bypass at 15°C produced an increase in intracellular pH in control and hyperglycemic animals (Fig 2). This is consistent with the observations of our group [5, 7] using a similar model. During the arrest period and through the first 20 minutes of reperfusion, the intracellular pH markedly decreased in both groups. Compared with the normoglycemic group, the hyperglycemic animals became significantly more acidotic. Intracellular pH returned to baseline after 30 minutes of reperfusion in the normoglycemic group but did not reach baseline until 1 hour of reperfusion in the hyperglycemic animals.

The ATP and PCr concentrations followed a course similar to that of pH. Hypothermic bypass resulted in increased levels of ATP and PCr in both groups, which subsequently decreased with circulatory arrest. Compared with the normoglycemic animals, the hyperglycemic group demonstrated significantly higher concentrations of ATP during hypothermic bypass and arrest (Fig 3). Repletion of ATP during the reperfusion period was similar for both groups.

Table 1. Changes in High-Energy Phosphates and Intracellular pH[a]

	pH_i		%Δ PCr		%Δ ATP	
Time	NG	HG	NG	HG	NG	HG
37°C	7.01 ± 0.03	7.01 ± 0.02	100	100	100	100
37°C CPB	7.01 ± 0.02	6.99 ± 0.05	99 ± 3	95 ± 4	99 ± 5	98 ± 3
15°C CPB	7.59 ± 0.02	7.56 ± 0.06	123 ± 5	125 ± 6	109 ± 5	115 ± 5[b]
Arrest (min)						
10	6.98 ± 0.26	7.17 ± 0.03	69 ± 10	78 ± 9	86 ± 4	107 ± 6[c]
30	6.58 ± 0.06	6.48 ± 0.05[d]	29 ± 5	30 ± 5	44 ± 4	62 ± 8[c]
50	6.48 ± 0.05	6.23 ± 0.07[c]	20 ± 4	20 ± 6	34 ± 5	40 ± 2[d]
Reperfusion (min)						
10	6.40 ± 0.08	6.08 ± 0.06[c]	60 ± 6	54 ± 7	67 ± 5	74 ± 7
30	6.97 ± 0.08	6.46 ± 0.23[c]	109 ± 6	87 ± 13[c]	92 ± 4	96 ± 6
50	7.03 ± 0.08	6.84 ± 0.18[b]	110 ± 6	97 ± 10[d]	93 ± 4	93 ± 4
70	7.07 ± 0.05	6.98 ± 0.15	113 ± 9	101 ± 15	90 ± 7	89 ± 6
90	7.11 ± 0.08	7.02 ± 0.14	112 ± 8	103 ± 13	89 ± 5	89 ± 6
110	7.07 ± 0.03	7.05 ± 0.14	112 ± 7	103 ± 14	90 ± 6	89 ± 8

[a] Data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ compared with normoglycemic group. [c] Significance: $p < 0.001$ compared with normoglycemic group. [d] Significance: $p < 0.01$ compared with normoglycemic group.

ATP = adenosine triphosphate; CPB = cardiopulmonary bypass; HG = hyperglycemia; NG = normoglycemia; PCr = phosphocreatine; pH_i = intracellular pH.

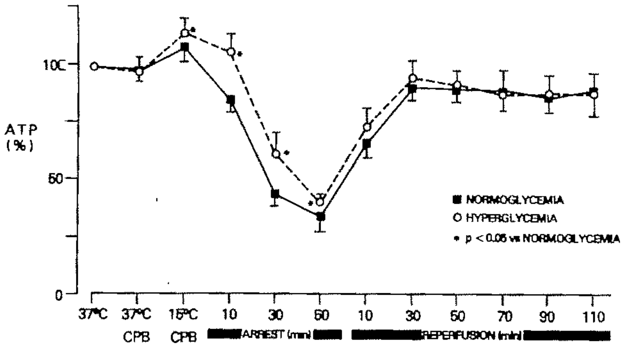


Fig 3. Percent change in cerebral adenosine triphosphate (ATP) *levels compared with baseline of* 100%. (CPB = *cardiopulmonary bypass.)*

Comment

Experimental studies based on models of focal and global normothermic cerebral ischemia have demonstrated a relationship between hyperglycemia, lactic acidosis, and cellular damage. It has been shown that the normothermic brain will exhaust all free-energy stores after as little as 2 minutes of complete ischemia [8]. After ATP depletion, anaerobic glycolysis metabolizes each glucose molecule into two ATP molecules, two lactate molecules, and two hydrogen ions, resulting in intracellular acidosis. Hyperglycemia will potentiate this reaction and result in increased lactate production and a further decrease in intracellular pH [4, 9]. Intracellular acidosis, in conjunction with other ischemia-induced alterations of cellular metabolism, produces dysfunction of ion-pumping enzyme systems, disruption of ion gradients, changes in membrane permeability, lipolysis, and proteolysis, and may lead to irreversible membrane damage [9]. Clinical data [10, 11] suggest that diabetic and nondiabetic patients in whom hyperglycemia develops after the onset of ischemic stroke have a worse neurological outcome than nondiabetic, normoglycemic patients.

The present study demonstrates that during hypothermic cerebral ischemia and early reperfusion, intracellular acidosis is exacerbated by hyperglycemia. Because the experimental design did not allow for the measurement of lactate concentrations, we are lacking direct evidence that increased anaerobic glycolysis and lactate accumulation is the primary mechanism of acidosis. Using ^{31}P and ^{1}H NMR spectroscopy, Corbett and colleagues [12] were able to demonstrate a linear relationship ($r = 0.94$) between intracellular pH and lactate levels in neonatal piglet brains during normothermic hemispheric ischemia. The linear relationship extended to lactate concentrations of 40 μmol/g. Using a similar model in adult cats, Gyulai and co-workers [13] reported a strong correlation between intracellular pH and brain lactate concentrations up to 20 μmol/g

In this study, both groups of animals exhibited increased levels of high-energy phosphates (ATP and PCr) during hypothermic CPB. As postulated by our group [5], this increase may be the result of a relative decrease in ATPase activity versus ATP synthesis (through glycolysis or oxidative phosphorylation) at low temperature. This would also explain the greater increase in ATP observed in the hyperglycemic animals (see Fig 3). During hypothermic bypass, increased levels of glucose might drive glycolysis and oxidative phosphorylation while ATPase activity is concurrently decreased, resulting in greater levels of ATP. With the onset of ischemia, hyperglycemia continues to drive glycolysis, resulting in a delayed decrease in ATP concentration and increased production of lactic acid.

Studies using rats and mice have demonstrated that hyperglycemia induced before normothermic ischemia significantly impairs postischemic recovery of brain energy metabolism. Gardiner and associates [14] subjected normoglycemic and hyperglycemic rats to 15 minutes of normothermic hemispheric ischemia by clamping the right carotid artery. Both groups experienced a substantial but similar decrease in PCr and ATP. Lactate concentration increased significantly in both groups, with the lactate levels in the hyperglycemic animals being much higher than in the normoglycemic group. Recovery of energy metabolism was significantly slower in the hyperglycemic group, and this was associated with a marked, persistent lactic acidosis. Using the same model, Welsh and co-authors [15] obtained similar results with mice.

Despite the greater severity and prolonged presence of acidosis in the hyperglycemic animals in this study, both groups exhibited nearly complete recovery of energy metabolism, a finding that leads us to conclude that major irreversible cell damage did not occur during ischemia and reperfusion. Hypothermia may have protected cellular integrity and preserved energy metabolism by slowing overall metabolism, thus making the cell less sensitive to acidosis and other ischemic insults. Although we have no evidence of cellular damage, it is conceivable that the areas of the sheep brain most susceptible to ischemia (which have not been defined) were not sampled by the NMR coil, which, in this model, was over the frontoparietal cortex. Moreover, it is possible that microinfarction occurred, but the extent was not great enough to significantly alter energy metabolism.

The uniform recovery of energy metabolism in both groups of animals may be explained in terms of a lactate threshold. Previous work using rats has shown that cerebral ischemia resulting in tissue lactate levels less than 16 μmol/g produces only selective neuronal damage in predictably vulnerable areas. Astrocytes and endothelial cells are spared, thus providing a protective effect by preventing widespread cerebral edema. With lactate levels greater than 16 μmol/g, astrocytes and endothelium as well as neurons are damaged, resulting in infarction and progressive cerebral edema [4]. Tissue lactate levels achieved in this model may have remained below a threshold level, resulting in minimal or no cell damage.

In summary, hyperglycemia resulted in increased cerebral intracellular acidosis during ischemia and reperfusion but did not adversely affect postischemic recovery of energy metabolism. Energy metabolism during the early ischemic period was enhanced by hyperglycemia. Further investigation is needed to define the relationship between acid-base metabolism and energy metabolism during hypothermia and hypothermic ischemia.

We thank Stephanie Sellers and Daryl Despres for the animal care assistance they provided.

References

1. Black PR, Van Devanter S, Cohn LH. Effects of hypothermia on systemic and organ system metabolism and function. J Surg Res 1976;20:49–63.
2. Weiland AP, Walker WE. Physiologic principles and clinical sequelae of cardiopulmonary bypass. Heart Lung 1986;15:34–9.
3. Mills NL, Beaudet RL, Isom OW, Spencer FC. Hyperglycemia during cardiopulmonary bypass. Ann Surg 1973;177:203–5.
4. Plum F. What causes infarction in the ischemic brain? The Robert Wartenberg Lecture. Neurology 1983;33:222–33.
5. Swain JA, McDonald TJ Jr, Balaban RS, Robbins RC. Metabolism of the heart and brain during hypothermic cardiopulmonary bypass. Ann Thorac Surg 1991;51:105–9.
6. Kost GJ. pH standardization for phosphorous-31 magnetic resonance heart spectroscopy at different temperatures. Magn Reson Med 1990;14:496–506.
7. Swain JA, McDonald TJ Jr, Robbins RC, Balaban RS. Relationship of cerebral and myocardial intracellular pH to blood pH during hypothermia. Am J Physiol 1991;260(Suppl):H1640–4.
8. Lowery OH, Passonneau JV, Hasselberger FX, Schulz DW. Effect of ischemia on known substrates and cofactors of the glycolytic pathway in brain. J Biol Chem 1964;239:18–30.
9. Siesjo BK, Wieloch T. Cerebral metabolism in ischaemia: neurochemical basis for therapy. Br J Anaesth 1985;57:47–62.
10. Pulsinelli WA, Levy DE, Sigsbee B, Scherer P, Plum F. Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus. Am J Med 1983;74:540–4.
11. Berger L, Hakim AM. The association of hyperglycemia with cerebral edema in stroke. Stroke 1986;17:865–71.
12. Corbett RJT, Laptook AR, Nunnally RL, Hassan A, Jackson J. Intracellular pH, lactate, and energy metabolism in neonatal brain during partial ischemia measured *in vivo* by ^{31}P and ^{1}H nuclear magnetic resonance spectroscopy. J Neurochem 1988;51:1501–9.
13. Gyulai L, Schnall M, McLaughlin AC, Leigh JS, Chance B. Simultaneous ^{31}P and ^{1}H nuclear magnetic resonance studies of hypoxia and ischaemia in the cat brain. J Cereb Blood Flow Metab 1987;7:543–51.
14. Gardiner M, Smith M, Kagstrom E, Shohami E, Siesjo BK. Influence of blood glucose concentration on brain lactate accumulation during severe hypoxia and subsequent recovery of brain energy metabolism. J Cereb Blood Flow Metab 1982;2:429–38.
15. Welsh FA, Sims RE, McKee AE. Effect of glucose on recovery of energy metabolism following hypoxia-oligemia in mouse brain: dose-dependence and carbohydrate specificity. J Cereb Blood Flow Metab 1983;3:486–92.

Clinical Cardiomyoplasty: Preoperative Factors Associated With Outcome

Anthony P. Furnary, MD, James A. Magovern, MD, Ignacio Y. Christlieb, MD, Judith E. Orie, MD, Kathleen A. Simpson, BS, and George J. Magovern, MD

Allegheny General Hospital, Allegheny-Singer Research Institute, and The Medical College of Pennsylvania, Pittsburgh, Pennsylvania

Dynamic cardiomyoplasty has been used clinically to augment the ventricular function of a failing heart. Fifteen clinical dynamic cardiomyoplasties have been performed at Allegheny General Hospital since 1985. Left ventricular ejection fraction improved in long-term survivors from a preoperative value of 0.23 ± 0.02 to 0.32 ± 0.05 with postoperative cardiomyostimulation ($p < 0.05$). There was an average reduction of 2 ± 0.3 New York Heart Association classes (3.6 ± 0.2 before operation versus 1.6 ± 0.4 after operation; $p < 0.001$). Postoperative mortality was 27% (4/15), and early mortality (within 6 months after operation) was 20% (3/15). Significant preoperative differences between survivors and nonsurvivors were found in right ventricular ejection fraction (0.53 ± 0.03 versus 0.30 ± 0.07; $p < 0.05$), pulmonary artery mean pressure (19 ± 2 versus 34 ± 6 mm Hg; $p < 0.05$), pulmonary artery diastolic pressure (12 ± 1 versus 25 ± 5 mm Hg; $p < 0.05$), and pulmonary vascular resistance (1.4 ± 2 versus 2.5 ± 0.7 Wood units; $p < 0.05$). Dynamic cardiomyoplasty can be done with low operative mortality in patients with isolated left ventricular failure, but mortality is high in those with biventricular failure or pulmonary hypertension. Improvement in functional class and ventricular function can be expected in long-term survivors. Application of these findings to patient selection will improve the risk/benefit ratio for dynamic cardiomyoplasty.

(Ann Thorac Surg 1992;54:1139–43)

Ventricular assist with autologous muscle tissue is an attractive potential adjunct therapy for heart failure. The disadvantages of mechanical circulatory assistance, such as thromboembolism and infection, and the shortcomings of cardiac transplantation, such as donor availability and immunosuppression, are avoided. In the research laboratory, skeletal muscle ventricles and muscle-powered assist devices are being developed, but application of these concepts to patients is not yet feasible. In the clinical setting, considerable attention has been drawn to cardiomyoplasty, a procedure in which the latissimus dorsi muscle is transposed into the chest, wrapped around the ventricles, and burst stimulated in synchrony with systole by an implantable stimulator.

Ninety-eight cardiomyoplasty operations had been reported worldwide as of February 1991 (M. Colson, Medtronic, Inc; personal communication); 15 were performed at Allegheny General Hospital. The operative technique has been well defined, but questions remain about patient selection and long-term results of the procedure. In this report, we analyze our initial clinical experience with the procedure to identify factors associated with a successful outcome.

Material and Methods

Fifteen patients underwent dynamic cardiomyoplasty at Allegheny General Hospital between September 1985 and January 1991. Patients were selected from the population referred to this hospital for management of congestive heart failure [1]. All had progression of heart failure despite maximal medical therapy, which included digoxin, diuretics, vasodilators, and angiotensin-converting enzyme inhibitors. None of the patients were suitable transplant candidates because of age, associated medical problems, or patient preference.

Patients with a previous left thoracotomy were excluded, as were those with complex or intractable arrhythmias. Major pulmonary dysfunction (forced expiratory volume in 1 second < 2 L/min), renal failure (creatinine clearance < 0.5 mL/s [30 mL/min]), and hepatic failure (severely abnormal liver enzyme values) were reasons for exclusion. Patients were not excluded because of age, although none were older than 65 years. Poor left ventricular function was not considered a reason for exclusion unless the patient was dependent on intravenous inotropic agents or a mechanical assist device.

Preoperative evaluation included a quality-of-life assessment and functional classification of the patient according to the New York Heart Association. Cardiac evaluation comprised the following: a careful history and physical examination; an electrocardiogram; two-dimensional, M-mode, and Doppler echocardiography; rest and exercise multigated acquisition scans; an exercise tolerance test with a thallium scan; and measurement of maximal oxygen consumption, peak heart rate, and blood pressure. Complete right and left heart catheterizations and 24-hour Holter monitor analysis were also performed.

Radiographic examinations included posteroanterior

Accepted for publication March 31, 1992.

Address reprint requests to Dr James A. Magovern, Department of Surgery, Allegheny General Hospital, 320 E North Ave, Pittsburgh, PA 15212.

© 1992 by The Society of Thoracic Surgeons

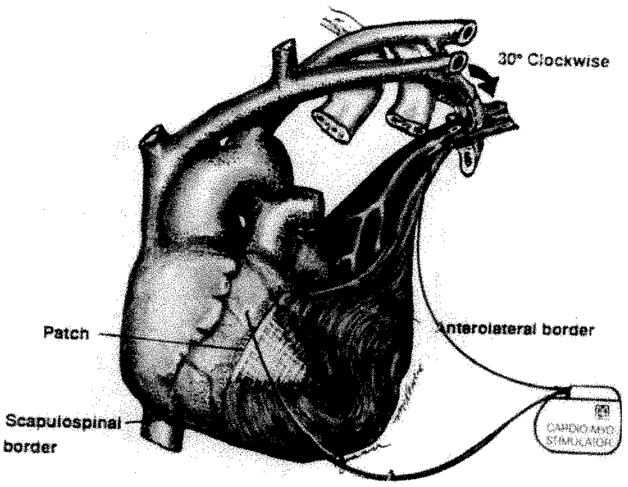


Fig 1. Posterior cardiocostal cardiomyoplasty.

and lateral chest roentgenograms with specific evaluation of the cardiothoracic ratio. A computed tomographic scan of the chest was performed to confirm the transverse cardiothoracic ratio, to calculate the cardiothoracic volumetric ratio, to identify the size and thickness of the latissimus dorsi muscles, and to rule out additional thoracic pathology. All patients also underwent full pulmonary function testing.

Selected studies were repeated at 6-month intervals during the postoperative follow-up period. All data were collected prospectively and analyzed retrospectively using two-tailed, paired and unpaired Student's t tests and Fisher's exact test. A p value of less than 0.05 was considered significant.

Operative Protocol

Cardiomyoplasty was performed using a single anesthetic in 5 patients. Ten patients underwent the procedure in two stages separated by several days. The latissimus dorsi was mobilized from the chest wall and subcutaneous tissue with care taken to preserve the neurovascular bundle [2]. Two intramuscular stimulating leads were threaded into the latissimus dorsi at right angles to muscle bundle orientation. The first was placed at the bifurcation of the thoracodorsal nerve and the other, approximately 6 cm distal and parallel to the first.

Several days later (in the two-stage procedure), the origin and insertion of the muscle were detached, and a 5-cm lateral portion of the second or third rib was removed. The latissimus was placed into the intrapleural space, and the tendinous portion of the muscle was sutured to the periosteum of the resected rib. Care was again taken to protect the neurovascular bundle.

The cardiac wrapping portion of the procedure was done through a midline sternotomy. The pericardium was opened, and the latissimus dorsi muscle was brought into the pericardial cavity. Cardiomyopathy is treated by encircling the ventricles with the muscle flap [3]. The most common muscle-wrapping technique is termed a left posterior cardiocostal wrap (Fig 1) [4]. The scapulospinal border of the left latissimus dorsi is sutured posteriorly to the pericardium at the level of the atrioventricular groove, starting inferior to the left pulmonary artery. The anterolateral border of the distal flap is then brought around the ventricles and sutured to itself on the anterior surface of the heart. The deep or "costal" surface of the muscle interfaces with the heart.

In cases of left ventricular aneurysm resection, the latissimus flap was employed to reinforce the aneurysm repair [5]. The muscle was placed directly over the ventricular defect in the anterior cardiocostal position (Fig 2) [4]. The costal surface of the muscle is in contact with the myocardium, but the anterolateral border runs along the anterior atrioventricular groove.

Eight of the 15 operations were performed using cardiopulmonary bypass for concomitant cardiac procedures (ventricular aneurysmectomy or coronary artery bypass grafting). In these patients, the wrap was done after release of the aortic cross-clamp but before weaning from the pump. When cardiomyoplasty was performed without cardiopulmonary bypass, it did not differ from the procedure just described. However, intraoperative arrhythmias and hypotension resulting from cardiac displacement were more frequent during positioning of the flap.

An epicardial sensing lead was attached to either ventricle for synchronization of muscle stimulation with ventricular contraction. This sensing lead and the intramuscular stimulation leads were connected to a Medtronic cardiomyostimulator (model SP1005; Medtronic Inc, Minneapolis, MN). The stimulation module was then positioned in a subfascial pocket on the anterior abdominal wall. The first 5 patients were operated on before the Medtronic SP1005 cardiomyostimulator was available, and therefore dual-chambered pulse generators were used.

A 6-week muscle-conditioning protocol was begun after a 2-week recovery period. This protocol was required to transform the muscle fibers of the latissimus dorsi from native glycolytic fast-twitch morphology (type II) to the nonfatigable oxidative slow-twitch (type I) variety [6]. Weekly incremental changes were made in the amplitude and frequency of the burst stimulus and the daily training

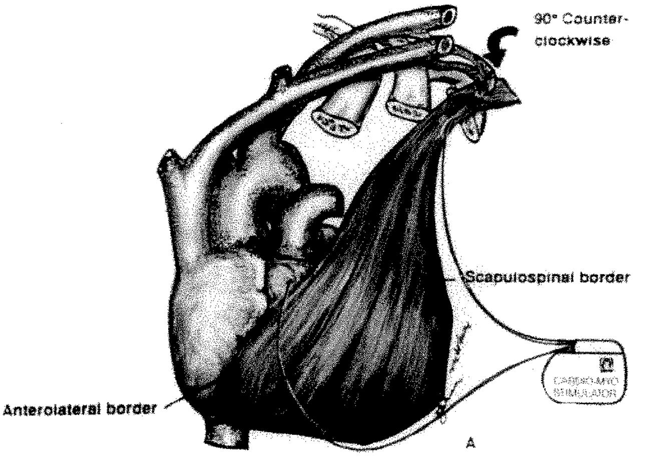


Fig 2. Anterior cardiocostal cardiomyoplasty.

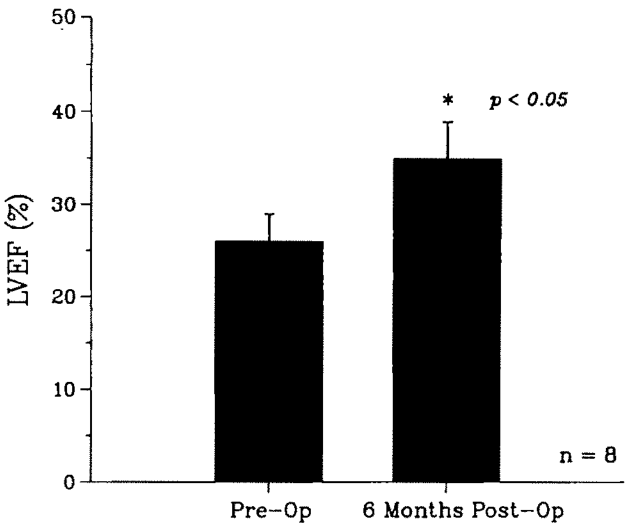


Fig 3. Mean postoperative left ventricular ejection fraction (LVEF) at 6 months with cardiomyostimulation was significantly improved in survivors as compared with the mean preoperative LVEF (n = 8).

duration until the final settings of 5 ± 1 V, 33 Hz, and 24-hour 1:1 pacing were achieved. Pulse width and burst duration remained constant at 210 microseconds and 185 milliseconds, respectively.

Results

Early and Late Mortality

There were four deaths within 30 days of operation, an operative mortality of 27%. Three of these deaths were secondary to progressive biventricular failure and occurred on postoperative days 2, 3, and 30. The fourth was due to a sudden ventricular arrhythmia on the 13th postoperative day.

The procedure has produced an initial hemodynamic disturbance in most patients. Inotropic support was used in 67% (10/15) of the patients, and 40% (6/15) required an intraaortic balloon pump. The average stay in the intensive care unit for operative survivors was 6.5 ± 1.5 days.

Eleven patients survived the operation. Three (27%) of them died within 6 months after operation, and 8 are long-term survivors. The causes of death were sudden death in 2 and progressive heart failure in 1. Concomitant operation did not have an effect on overall survival, as 5 of 8 of these patients survived compared with 3 of 7 patients with isolated cardiomyoplasty ($p =$ not significant by Fisher's exact test). The 8 remaining patients have a mean survivorship of 36 ± 9 months (range, 7 to 76 months).

Postoperative Cardiac Function

The cardiac functional status of the 8 long-term survivors has been evaluated at 6-month intervals. Mean resting left ventricular ejection fraction measured by multigated acquisition radionuclide scan improved from a preoperative value of 0.24 ± 0.04 to 0.32 ± 0.05 at 6 months ($p < 0.05$) (Fig 3). Postoperative resting left ventricular ejection fraction at 6 and 12 months with the stimulator off was 0.28 ± 0.04 compared with 0.32 ± 0.05 with the device on ($p < 0.05$), yielding a 16% relative increase in resting left ventricular ejection fraction with cardiomyostimulation. Six of the 8 long-term survivors had repeat cardiac catheterization. No consistent changes in hemodynamic variables were detected.

Before operation, 4 patients were in New York Heart Association functional class III and 11, in class IV (mean functional class, 3.7 ± 0.1). All the patients who survived the operation improved by at least one functional class, with an average improvement of 2.0 ± 0.3 classes ($p < 0.001$). All long-term survivors are in functional class I or II (mean functional class, 1.6 ± 0.4), and all report a decreased physical tolerance when their muscular stimulators are turned off for more than a few hours.

Analysis of Clinical Results

Preoperative evaluation data for all patients were retrospectively examined to identify differences between survivors and nonsurvivors. These data are presented in Table 1. No differences were detected in age, sex, pulmonary capillary wedge pressure, maximum work, peak double product, end-diastolic volume, or cardiothoracic ratio. Significant differences between long-term survivors and nonsurvivors were found in preoperative right ventricular ejection fraction, pulmonary artery mean pressure, pulmonary artery diastolic pressure, pulmonary vascular resistance, and cardiac index.

Although all patients in this series had left ventricular failure, 6 had concomitant right ventricular failure (right ventricular ejection fraction < 0.40). In this group with preoperative biventricular failure, there were three perioperative deaths and no long-term (>6 months) survivors. However, 8 of the 9 patients with isolated left ventricular failure were long-term survivors. Pulmonary hypertension, defined as a pulmonary artery mean pressure greater than 30 mm Hg or pulmonary vascular resistance greater than 3 Wood units, also had an adverse effect on survival. Only 3 of the 5 patients with pulmonary hypertension survived the operation, and none were long-term survivors (Table 2).

Comment

Chronic congestive heart failure is a major national health problem with 2.3 million cases contributing to more than 400,000 deaths annually in the United States [7]. At present, the best surgical therapy for end-stage congestive heart failure is orthotopic heart transplantation. The limited donor supply, the effects of immunosuppression, and a 5-year survival rate of 60% [8] make this treatment less than optimal. Mechanical circulatory assist devices are in use but face problems of high cost, thromboembolism, infection, and mechanical failure.

The envisioned advantages of cardiomyoplasty are promising as compared with the treatments just mentioned. There is an unlimited "donor supply," as nearly all patients have a functional latissimus dorsi muscle that can be transposed onto the heart. Immunosuppression is not required. No artificial materials are in contact with the blood; hence, the risk of thromboembolism is not in-

Table 1. Comparison of Preoperative Evaluation Data as a Function of Long-Term Survival[a]

Variable	Long-Term Survival[b] Yes (n = 8)	Long-Term Survival[b] No (n = 7)	*p* Value
Age (y)	56 ± 3	56 ± 3	NS
Sex (M:F)	4:4	5:2	NS
Maximum oxygen consumption (treadmill; METs)	4.9 ± 2.1	2.0 ± 0.5	NS
Peak double product	16,283 ± 1,538	15,312 ± 2,244	NS
End-diastolic volume (mL)	421 ± 47	399 ± 67	NS
Cardiothoracic ratio	0.55 ± 0.03	0.61 ± 0.02	NS
Pulmonary artery mean pressure (mm Hg)	19 ± 2	34 ± 6	0.05
Pulmonary artery diastolic pressure (mm Hg)	12 ± 1	25 ± 5	0.05
Pulmonary capillary wedge pressure (mm Hg)	12 ± 1	24 ± 7	NS
Pulmonary vascular resistance (Wood units)	1.4 ± 0.2	2.5 ± 0.7	NS
Left ventricular end-diastolic pressure (mm Hg)	20 ± 2	24 ± 4	NS
Left ventricular ejection fraction	0.26 ± 0.03	0.22 ± 0.03	NS
Right ventricular ejection fraction	0.53 ± 0.03	0.30 ± 0.07	0.05
Cardiac index ($L \cdot min^{-1} \cdot m^{-2}$)	3.1 ± 0.4	2.0 ± 0.2	0.05
Concomitant operation	5/8	3/7	NS

[a] All continuous data are shown as the mean ± the standard error of the mean. [b] Survival for more than 6 months postoperatively.

METs = metabolic equivalents; NS = not significant.

creased. The risks of infection and device failure are low and comparable with those of cardiac pacemaker or automatic implantable cardioverter defibrillator implantation [9]. Most importantly, should cardiomyoplasty fail to improve the patient's functional status, the options of mechanical circulatory assist or orthotopic transplantation can still be exercised.

It has long been known that patients with congestive heart failure are a high-risk group for major surgical procedures because of poor cardiac reserve and associated medical problems [7]. Unlike transplantation and circulatory assist, the hemodynamic benefits obtained from cardiomyoplasty are not immediate because time is required to complete the muscle-conditioning process. Because of this hiatus, Chachques and associates [10] suggested that potential patients should have some "cardiac reserve" to help them through the conditioning period. The compiled worldwide results, which show a higher mortality for patients in New York Heart Association class IV than those in class III (33% versus 12%), support this theory [11]. Our analysis of survivorship characteristics also demonstrates that patients undergoing cardiomyoplasty have a better outcome if they have some preservation of cardiac function.

Biventricular heart failure in this patient population is a predictor of an unfavorable outcome. None of the 6 patients with this condition were long-term survivors. These patients have a poor prognosis with medical therapy [12], and, based on current knowledge, it appears that they achieve little benefit from cardiomyoplasty using the left latissimus dorsi muscle. Cardiac transplantation should be the procedure of choice for patients with advanced biventricular failure.

Pulmonary hypertension (pulmonary artery mean pressure > 30 mm Hg, pulmonary artery diastolic pressure > 20 mm Hg, or pulmonary vascular resistance > 3 Wood units) is not modified by cardiomyoplasty and therefore is a relative contraindication to the procedure as now practiced. This is also true in the case of cardiac transplantation, which carries a high risk in similar patients with fixed pulmonary hypertension [13]. In these patients, the only surgical options may be heart-lung transplantation or a mechanical ventricular assist device.

This cohort of 15 patients represents our early experience with this experimental procedure. Given this small sample size, these results should be viewed with caution. Multivariate risk-factor analyses cannot be performed until a greater number of patients are enrolled. Therefore, these findings are presented with the caveat that further validation is required, with analysis of data from a larger, perhaps worldwide clinical trial.

The Allegheny General Hospital experience suggests that a left latissimus dorsi cardiomyoplasty is best suited for patients with left ventricular failure who do not have major pulmonary hypertension or right ventricular fail-

Table 2. Cardiomyoplasty Survival Results Associated With Preoperative Cardiopulmonary Status

Variable	No. of Patients	Operative Survival	Long-Term Survival
Isolated left ventricular failure (RVEF > 0.40)	9	8/9	8/9
Biventricular failure (RVEF < 0.40)	6	3/6	0/6
Pulmonary hypertension (mean PAP > 30 mm Hg or PVR > 3 Wood units)	5	3/5	0/5

PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; RVEF = right ventricular ejection fraction (resting).

ure. Most of these patients will also be in New York Heart Association class III. This subset of patients has had an objective improvement in rest and exercise left ventricular ejection fraction as well as a definite improvement in subjective exercise tolerance. Both have been achieved with low morbidity and mortality (11%). Recent laboratory data [14] indicate that a right anterior cardiocostal cardiomyoplasty can provide significant biventricular augmentation of a nondepressed canine heart. This may become a useful option for the patient with biventricular failure.

Cardiomyoplasty remains an experimental procedure. The initial experience with cardiomyoplasty both here and in France [15] has produced a higher than anticipated mortality. This result is similar to that in the early days of cardiac transplantation or aortic valve replacement, when the mixed results of these promising new procedures were subject to the skeptical scrutiny of the medical community. However, perseverance with the procedure and critical analysis of the results will allow a more precise definition of the specific indications for cardiomyoplasty. The risk/benefit ratio of the operation should improve with better patient selection criteria and continued improvements in the technical aspects of the operation.

This work was supported in part by Public Health Service grant HL38078.

We thank Dr Richard E. Clark for his editing and advice and Ms Dinean Samuel for her assistance in the preparation of this manuscript.

References

1. Magovern JA, Furnary AP, Christlieb IY, Kao RL, Park SB, Magovern GJ. Indications and risk analysis for clinical cardiomyoplasty. Semin Thorac Cardiovasc Surg 1991;3:145–8.
2. Heckler FR, White MJ. Isolation of skeletal muscle for biomechanical circulatory assist. Semin Thorac Cardiovasc Surg 1991;3:128–31.
3. Magovern GJ, Heckler FR, Park SB, et al. Paced skeletal muscle for dynamic cardiomyoplasty. Ann Thorac Surg 1988; 45:614–9.
4. Furnary AP, Christlieb IY, Magovern JA, Magovern GJ. A standardized nomenclature for latissimus dorsi cardiomyoplasty. J Cardiac Surg 1991;6:74–9.
5. Magovern GJ, Heckler FR, Park SB, et al. Paced latissimus dorsi used for dynamic cardiomyoplasty of left ventricular aneurysms. Ann Thorac Surg 1987;44:379–88.
6. Eisenberg BR, Salmons S. The reorganization of subcellular structure in muscle undergoing fast-to-slow type transformation. A stereological study. Cell Tissue Res 1981;220:449–71.
7. Smith WM. Epidemiology of congestive heart failure. Am J Cardiol 1985;55:3A–8A.
8. Baumgartner WA. Comparative results and future implications of heart transplantation. In: Baumgartner WA, Reitz BA, Achuff SC, eds. Heart and heart-lung transplantation. Philadelphia: Saunders, 1990:390–6.
9. Furman S. Implantable cardioverter defibrillator statistics. PACE 1990;13:1–2.
10. Chachques JC, Grandjean P, Schwartz K, et al. Effect of latissimus dorsi dynamic cardiomyoplasty on ventricular function. Circulation 1988;78(Suppl 3):203–16.
11. Grandjean PA, Austin L, Chan S, et al. Dynamic cardiomyoplasty clinical follow-up results. J Cardiac Surg 1991;6:80–8.
12. The Consensus Trial Study Group. Effects of enalopril on mortality in severe congestive heart failure. N Engl J Med 1987;316:1429–35.
13. Murali S, Estrada-Quintero T, Kormos RL, et al. Hemodynamic evaluation of cardiac transplant patients immunosuppression with FK506. J Heart Lung Transplant 1991;10(Suppl 1):176.
14. Furnary AF, Magovern JA, Christlieb IY, Trumble DR. Improved ventricular augmentation with right latissimus cardiomyoplasty. Surg Forum 1991;42:307–9.
15. Carpentier A, Chachques JC. Clinical dynamic cardiomyoplasty: method and outcome. Semin Thorac Cardiovasc Surg 1991;3:136–9.

Fluosol Cardioplegia Results in Complete Functional Recovery: A Comparison With Blood Cardioplegia

Jeffrey M. Pearl, MD, Hillel Laks, MD, Davis C. Drinkwater, MD,
Avedis Meneshian, BS, Steven M. Martin, MD, Mark Curzan, MS, and
Paul A. Chang, BS

Division of Cardiothoracic Surgery, Department of Surgery, The University of California, Los Angeles, California

Blood cardioplegia is considered by many to be the preferred solution for myocardial protection. Proposed benefits include the ability to deliver oxygen and the ability to maintain metabolic substrate stores. However, the decreased capacity of blood to release oxygen at hypothermic conditions as well as the presence of deleterious leukocytes, platelets, and complement may limit complete functional recovery. Fluosol is an asanguineous solution with the ability to bind and release oxygen linearly at low temperatures. Neonatal piglet hearts (24 to 48 hours old) were excised and supported on an isolated, blood-perfused working heart model. After baseline stroke-work index was determined, hearts were arrested with either normocalcemic blood cardioplegia (group 1, n = 8) or normocalcemic Fluosol cardioplegia (group 2, n = 8). Cold cardioplegia was administered at 45 mm Hg every 20 minutes for 2 hours. Hearts were then reperfused with whole blood. Functional recovery, expressed as percent of control stroke-work index, was determined 60 minutes after reperfusion at left atrial pressures of 3, 6, 9, and 12 mm Hg. Functional recovery at 60 minutes was similar between group 1 (95%, 93%, 93%, 88%) and group 2 (100%, 94%, 94%, 95%) at left atrial pressures of 3, 6, 9, and 12 mm Hg, respectively. Mean lactate consumption 5 minutes after reperfusion was significantly greater ($p = 0.0001$) in group 1 ($31.8 \pm 6.3\ \mu g \cdot min^{-1} \cdot g^{-1}$) than in group 2 ($-0.59 \pm 0.1\ \mu g \cdot min^{-1} \cdot g^{-1}$), indicating superior metabolic recovery in the blood cardioplegia hearts. Edema formation, as determined both by water content (group 1, 81.10%; group 2, 81.63%) and by electron microscopy, was not significantly different between groups. Tissue adenosine triphosphate levels 1 hour after reperfusion were also not significantly different. In conclusion, similar to blood cardioplegia, Fluosol results in complete functional recovery after cold ischemic arrest, despite inferior metabolic recovery. Because of the absence of injurious blood elements, Fluosol with added substrate may have a role as a cardioplegic agent when preoperative ischemia or hypoxia exists.

(Ann Thorac Surg 1992;54:1144–50)

Blood cardioplegia has been accepted by many as the optimal cardioplegic agent for both adult and pediatric myocardial protection [1–6]. In addition to its ability to deliver oxygen, blood contains glucose, amino acids, natural buffers, and other metabolic substrates and is readily available [6]. Numerous studies [2–7] comparing blood cardioplegia with various crystalloid solutions have documented superior functional [4] and metabolic recovery [2, 5, 8] and preserved ultrastructure [6]. However, blood does contain potentially injurious elements, such as leukocytes, platelets, and complement, that can be activated both during initial cardioplegia induction and during repeated administrations of blood cardioplegia [9, 10]. Leukocyte-mediated injury can occur with the initial dose of blood cardioplegia when preoperative ischemia or hypoxia exists [10]. Leukocyte depletion, which has been applied both in the laboratory [11–13] and clinically, is cumbersome and does not consistently remove platelets or complement. Nonetheless, studies [11–13] using leukocyte-depleted blood cardioplegia as a reperfusate after ischemic arrest have shown improved recovery over whole-blood cardioplegia.

Acellular, oxygenated perfluorochemical solutions such as Fluosol (Green Cross Corp, Osaka, Japan) are considered to be potentially useful agents for reperfusion of the ischemic myocardium [14, 15]. Previous studies [15, 16] have demonstrated a decreased infarct size when ischemic myocardium is first reperfused with Fluosol instead of blood. Only recently has Fluosol been applied clinically as a reperfusate during coronary angioplasty, and although variable, initial results support both its safety and efficacy [14, 17–20]. Recent work [21] in our laboratory has also documented Fluosol's ability to decrease reperfusion injury after 12 hours of cold ischemic arrest.

Unlike oxygenated crystalloid solutions or blood cardioplegia, Fluosol actively binds and releases oxygen linearly at all temperatures, giving it the ability to supply oxygen under hypothermic conditions [16, 22; Martin SM, Laks

---

Accepted for publication March 31, 1992.

Address reprint requests to Dr Laks, Division of Cardiothoracic Surgery, UCLA Medical Center, CHS 62-182-A, 10833 LeConte Ave, Los Angeles, CA 90024.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

H, Drinkwater DC, et al; unpublished observations]. This may prove beneficial when it is used as an intermittent cardioplegic agent.

In view of Fluosol's unique oxygen-delivery characteristics and proven ability to prevent reperfusion injury, a study was undertaken to determine its potential usefulness as a cardioplegic agent.

Material and Methods

Experimental Preparation

Adult support pigs were initially anesthetized with ketamine hydrochloride (2,000 mg) and acepromazine maleate (30 mg); after a tracheotomy, they were ventilated with a volume ventilator set at an inspired oxygen fraction of 1. Anesthesia was maintained with a constant infusion of sodium pentobarbital (6 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$). Mechanical ventilation was adjusted to maintain a carbon dioxide tension of 30 to 35 mm Hg, an oxygen tension of greater than 400 mm Hg, and an arterial pH of 7.40 to 7.50; sodium bicarbonate was added as necessary to correct metabolic acidosis. Mean systemic blood pressure was maintained between 70 and 80 mm Hg by administration of intravenous fluid (lactated Ringer's). Arterial blood was supplied to the perfusion circuit from the femoral artery of the support pig; the femoral vein was used for the venous return.

Sixteen newborn piglets (Duroc), 24 to 48 hours old, were anesthetized with intramuscular ketamine (250 mg) and acepromazine (5 mg). A tracheotomy was performed and mechanical ventilation instituted. The heart and great vessels were exposed through a median sternotomy. The hemiazygos vein and the left subclavian artery were ligated; the descending thoracic aorta, the innominate artery, the superior and inferior venae cavae, and the pulmonary artery were encircled. The aortic root was perfused via a cannula in the innominate artery through which aortic root pressure was monitored continuously and maintained at 50 mm Hg. The superior and inferior venae cavae were ligated and divided, the descending aorta was cross-clamped, and the main pulmonary artery was opened and cannulated to drain coronary sinus blood. The pulmonary veins and the aorta distal to the cross-clamp were divided, thereby completing the isolation. The perfused, beating heart was excised and connected to the perfusion circuit.

The aorta was cannulated and connected to an open column of tubing to maintain a constant aortic root pressure of 80 mm Hg. If present, a patent ductus arteriosus or patent foramen ovale was closed. The left atrium was cannulated with an infusion cannula that delivered blood from a separately controlled infusion pump (Shiley Incorporated, San Diego, CA) and reservoir. A fiberoptic transducer-tipped catheter in the left atrial cannula was connected to the preamplifier (models 110-4 and 420; Camino Laboratories, San Diego, CA). The fiberoptic catheter (outside diameter, 1.3 mm) was advanced into the left atrium, and a second catheter was advanced into the left ventricle. Preamplifier output was delivered to a Gould transducer amplifier (model 13-4615-50; Gould Inc, Cleveland, OH), and the signal was recorded on an Astromed MT-9000 chart recorder (Astromed, Inc, West Warwick, RI). Arterial blood gas analysis of the support pig was done every 15 minutes (ABL-1; Radiometer A/S, Copenhagen, Denmark).

Baseline Measurements

After 10 minutes in the working mode on the perfusion circuit, control ventricular function was evaluated at 37°C by infusing blood into the left atrium and measuring the cardiac output at progressively increased mean left atrial pressures. Baseline function for each heart was defined as the left ventricular stroke work index (erg/g) calculated at mean left atrial pressures of 3, 6, 9, and 12 mm Hg:

$$\text{SWI} = \frac{(\text{MAP} - \text{LVEDP}) \times \text{CO}}{\text{HR} \times \text{Wt}} \times 1333$$

where SWI is the stroke-work index, MAP is the mean aortic root pressure (80 mm Hg), LVEDP is the left ventricular end-diastolic pressure, CO is the cardiac output (mL/min), HR is the heart rate (beats/min), and Wt is the heart weight (g).

Induction and Maintenance of Cardiac Arrest

After evaluation of baseline hemodynamic function, the left atrial cannula was removed, the innominate pump turned off, and the aortic perfusion cannula clamped. Cardiac arrest was obtained by infusion of 4°C cardioplegia at 50 mm Hg through the innominate cannula for 2 minutes. Topical hypothermia was also employed. Cardioplegia infusion was repeated every 20 minutes for 2 hours. A needle thermistor-tipped probe was inserted into the right ventricle at the base of the pulmonary artery for continuous monitoring of the myocardial temperature (Shiley DPM). During the period of arrest, the myocardial temperature was maintained between 8° and 10°C by submersion in cold saline slush.

The 16 piglet hearts were randomized into two groups according to the type of myocardial protection used. Group 1 ($n = 8$) received normocalcemic blood cardioplegia, and group 2 ($n = 8$) received normocalcemic, oxygenated perfluorochemical cardioplegia (Fluosol). The concentration of Fluosol is 20% by weight or 10% by volume, which is the standard manufactured concentration. The composition of the two cardioplegic solutions is given in Table 1. The concentrations of sodium, calcium, and potassium were very similar between the two solutions. The osmolarity was higher and the pH at 10°C lower in the Fluosol cardioplegia.

Reperfusion

After 2 hours of cold ischemic arrest, the aortic root was reperfused with warm whole blood (38°C) at a pressure of 50 mm Hg until mechanical activity resumed (oxygen tension, 400 to 500 mm Hg; hematocrit, 0.25 to 0.30). Aortic root pressure was then increased to 80 mm Hg. Defibrillation was performed when necessary with 5 J of direct-current countershock. Twenty minutes after reperfusion, the left atrial cannula was reinserted and the heart placed in the working mode.

Table 1. Composition of Cardioplegic Solutions[a]

Component	Blood	Fluosol
pH	7.8	7.35
Pco_2 (mm Hg)	17	70
Po_2 (mm Hg)	454	924
O_2 content (vol/100 mL)	12	6
Na (mEq/L)	130	144
K (mEq/L)	22/10[b]	22.5
Ca (mmol/L)	1.1	1.1
Cl (mEq/L)	110	115
Osmolarity	330	454
Glucose (mg/dL)	>400	320

[a] Note similarities in electrolyte composition, including calcium. Blood cardioplegia had an O_2 content twice that of Fluosol. [b] The KCl concentration was 20 to 22 mEq in the initial dose and 8 to 10 mEq in all subsequent doses.

Pco_2 = carbon dioxide tension; Po_2 = oxygen tension.

Hemodynamic Measurements After Reperfusion

Thirty and 60 minutes after reperfusion, left ventricular stroke-work index and coronary blood flow were determined at mean left atrial pressures of 3, 6, 9, and 12 mm Hg.

Metabolic Recovery

Coronary blood flow 5 minutes after reperfusion was measured, and arterial and coronary venous samples were obtained for lactate analysis to assess metabolic recovery. After completion of the 60-minute hemodynamic measurements, biopsy samples were obtained from the anterior left ventricular wall for adenosine triphosphate and creatine phosphate assessment.

Ultrastructure and Histology

A left ventricular biopsy specimen was obtained 60 minutes after reperfusion for electron microscopy. An additional biopsy sample was obtained for water content, which was compared with established control values. Ultrastructural injury was graded using established criteria and assigned a score of 1 to 4, with 4 representing severe injury and 1 representing minimal injury. This was compared with a previously established mean control value of 0.5.

High-Energy Phosphate and Lactate Analysis

Extraction was carried out with 3 mol/L $HClO_4$ in a cool methanol bath. Adenine nucleotides were measured by high-pressure liquid chromatography (Waters Inc, South San Francisco, CA). Creatine phosphate was measured by enzymatic method with a fluorometer (model 112; Turner Inc, Mountain View, CA) [23]. Lactate was determined by enzymatic method (260-110; Sigma Chemical, St. Louis, MO).

Statistical Analysis

Results were expressed as the mean ± the standard error of the mean. The two-tailed paired Student's t test was used to compare preischemic and postischemic stroke-work index, so that each subject served as its own control. The two-tailed unpaired Student's t test was used to compare postischemic recovery as well as water content, lactate consumption, and high-energy phosphate levels between the two groups. A p value of less than 0.05 was considered significant.

Animal Care

All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

Results

Delivery of Cardioplegia

Ventricular activity in both groups was arrested within 20 seconds of cardioplegia administration. Myocardial temperature was maintained between 8° and 10°C in all hearts. Cardioplegia was administered at a constant pressure and time; hence cardioplegia dose was a measure of coronary vascular resistance and cardioplegia viscosity. Hearts in group 1 received a mean of 3.3 mL per gram of heart tissue per dose, and hearts in group 2 received 4.8 mL per gram of heart tissue per dose. The viscosity of Fluosol is less than that of blood, which was most likely responsible for this difference.

Functional Recovery

On average, electrical activity developed 1.5 minutes after reperfusion in group 1 hearts, whereas in hearts in group 2, electrical activity developed almost immediately on reperfusion (mean time, 10 seconds) ($p < 0.05$). Defibrillation was required in 7 of the 8 hearts in group 1 versus 3 of the 8 in group 2. Preischemic stroke-work index was not significantly different between groups, and postischemic stroke-work index in groups 1 and 2 was not significantly different from the preischemic values both 30 and 60 minutes after reperfusion (Figs 1, 2). Functional recovery at 30 minutes was 91%, 94%, 94%, and 89% in group 1 and 97%, 93%, 96%, and 96% in group 2 at left atrial pressures of 3, 6, 9, and 12 mm Hg, respectively (Fig 3). Similarly, 60-minute recovery was 95%, 93%, 93%, and 88% in group 1 and 100%, 94%, 94%, and 95% in group 2 at left atrial pressures of 3, 6, 9, and 12 mm Hg, respectively (Fig 4). Percent functional recovery was unchanged between 30 and 60 minutes in both groups. In group 1, the postreperfusion Starling curves tended to be flat, whereas in group 2, they were similar to prearrest curves. This finding provides indirect evidence of diastolic dysfunction in group 1, which does not appear to be present in group 2.

Coronary Blood Flow

Coronary blood flow measured 5 minutes after reperfusion was not significantly different between groups 1 and 2, 3.2 $\mathrm{mL \cdot g^{-1} \cdot min^{-1}}$ versus 3.1 $\mathrm{mL \cdot g^{-1} \cdot min^{-1}}$, re-

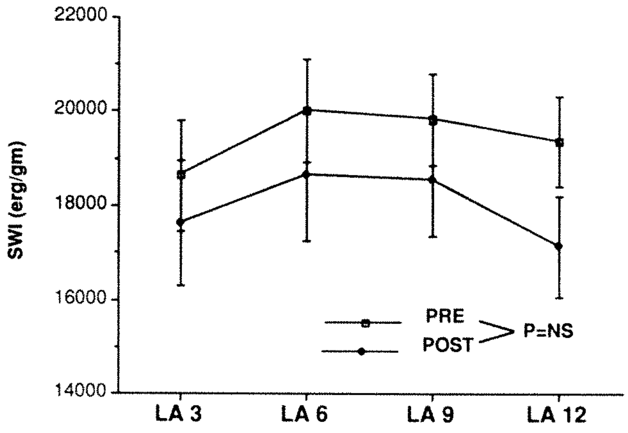


Fig 1. Stroke-work index (SWI) 60 minutes after reperfusion did not differ significantly from preischemic values in hearts protected with blood cardioplegia. (LA = *left atrial pressure;* NS = *not significant.*)

spectively. In both groups, blood flow at 5 minutes was 60% greater than baseline values, indicating a postischemic coronary vasodilatory response. By 60 minutes after reperfusion, coronary blood flow returned to near baseline values in both groups (Fig 5).

Water Content

Water content at the conclusion of the reperfusion period was not significantly different between group 1 (81.10%) and group 2 (81.63%) (p = 0.176) (Fig 6). These values represent only a slight increase over baseline water content (80.4%) from nonischemic controls previously analyzed in our laboratory. Therefore, both solutions result in only mild increases in myocardial edema during ischemic arrest.

Ultrastructural Injury

Hearts in both groups showed only minor ultrastructural changes consisting of mild to moderate enlargement of nuclei, nuclear chromatin clumping, and mild interstitial edema. There was no noticeable difference in ultrastructural appearance between hearts in group 1 and those in group 2 at the conclusion of the study. The mean injury score in both groups (1.4) was slightly but significantly (p = 0.05) worse than that for nonischemic controls (mean score, 0.5).

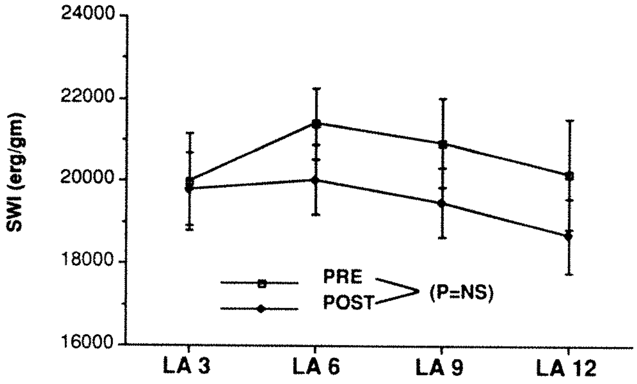


Fig 2. Stroke-work index (SWI) 60 minutes after reperfusion was not significantly different from preischemic values in the hearts protected with Fluosol. (LA = *left atrial pressure;* NS = *not significant.*)

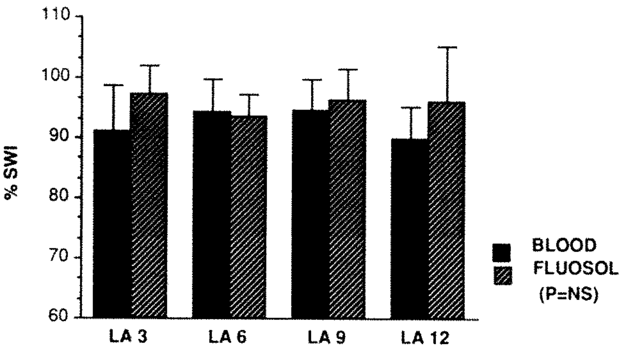


Fig 3. Percent functional recovery was close to 100% in both groups at 30 minutes. There was no significant decrease in recovery at higher left atrial pressures (LA), *indicating preserved diastolic function and compliance.* (NS = *not significant;* SWI = *stroke-work index.*)

Lactate Consumption

Lactate consumption was significantly greater in group 1 than in group 2 5 minutes after reperfusion: 31.8 ± 6.26 $\mu g \cdot min^{-1} \cdot g^{-1}$ in group 1 versus −0.59 ± 0.1 $\mu g \cdot min^{-1} \cdot g^{-1}$ in group 2 (p = 0.0001) (Fig 7). Preoperative lactate consumption in both groups before arrest was 26.4 ± 4.42 $\mu g \cdot min^{-1} \cdot g^{-1}$.

Adenosine Triphosphate and Creatine Phosphate Levels

Sixty minutes after reperfusion, there was no significant difference in tissue adenosine triphosphate levels: 17.04 ± 1.4 μmol/g of dry heart tissue in group 1 and 15.5 ± 3.8 μmol/g of dry heart tissue in group 2 (p = 0.62). Tissue creatine phosphate levels were also not significantly different between group 1 (25.7 ± 3.9 μmol/g of dry heart tissue) and group 2 (30.0 ± 3.9 μmol/g of dry heart tissue) (p = 0.45). Nonischemic control values for adenosine triphosphate and creatine phosphate in our laboratory are 14 ± 2 and 32 ± 4 μmol/g of dry heart tissue, respectively.

Comment

Neonatal Myocardial Protection

Blood cardioplegia has been shown both experimentally and clinically to be superior to crystalloid cardioplegia for myocardial protection [1–4, 6]. The majority of research supporting the benefits of blood cardioplegia has been carried out in adolescent or adult animals and humans and empirically applied to the newborn and infant [3, 4–6]. It has been suggested that because of increased glycogen stores and glycogenolytic activity, the infant heart tolerates ischemia or hypoxia better than the adult heart [24, 25]. However, studies [26–28] restricted to newborn myocardium, defined as less than 5 to 7 days of age, have demonstrated that despite the use of blood cardioplegia, complete functional recovery is not obtained after a period of cold ischemic arrest. Pridjian and col-

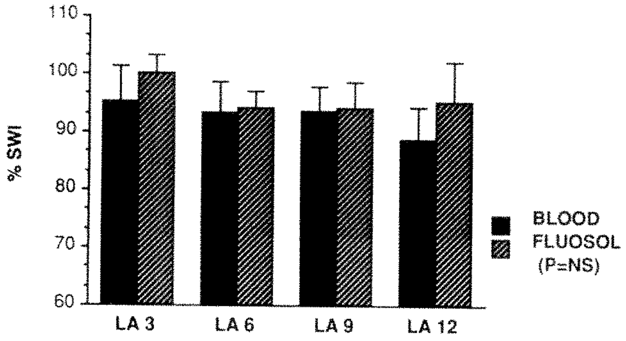


Fig 4. Percent functional recovery was slightly better in group 2 (Fluosol) at 60 minutes, but the differences were not significant (NS). There was no loss of function between 30 and 60 minutes. (LA = left atrial pressure; SWI = stroke-work index.)

leagues [25] concluded that whereas the infant heart (older than 10 days) is the least vulnerable to ischemia, the immature newborn heart is the most vulnerable. The presence of preoperative cyanosis may further increase the vulnerability of the newborn myocardium to an ischemic period [26].

Clinical experience in the cyanotic newborn and infant supports the experimental data that protection of the immature, newborn myocardium is suboptimal [29, 30]. With increasing numbers of patients with congenital heart disease undergoing cardiac repair in the first few days of life, a search for improved methods of myocardial protection is certainly warranted.

Adult Myocardial Protection

Although current methods of myocardial protection with antegrade and retrograde blood cardioplegia are adequate in adult cardiac operations, patients with preoperative ischemia are still prone to myocardial stunning and poor ventricular recovery after urgent revascularization [6]. Failure of myocardial recovery may be related to reperfusion injury, which can occur both with induction of cardioplegic arrest or with cardioplegic reperfusion after revascularization.

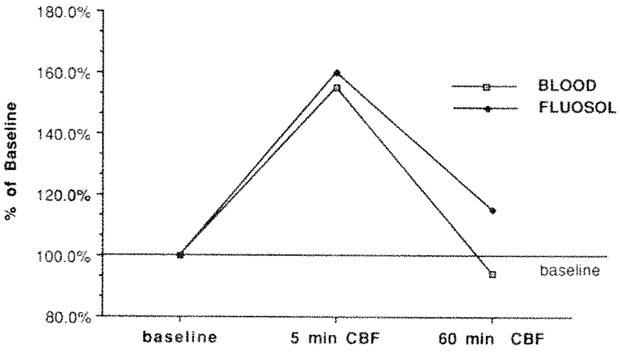


Fig 5. Coronary vascular resistance as determined from coronary blood flow (CBF) was 60% greater than baseline in both groups after reperfusion, indicating a postischemic coronary vasodilatory response. Coronary vascular resistance was near normal values 60 minutes after reperfusion.

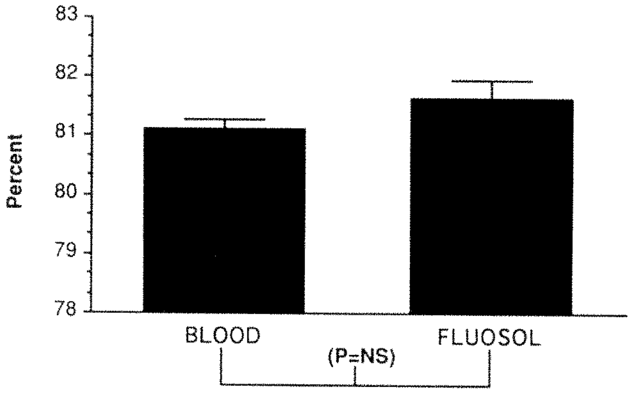


Fig 6. Water content 60 minutes after reperfusion was not significantly different between the two groups and was only marginally elevated compared with control values. (NS = not significant.)

Oxygenated Cardioplegia: Fluosol Versus Blood Cardioplegia

Oxygenated cardioplegic solutions have been shown to provide superior functional and metabolic recovery over unoxygenated solutions and have extended the safe period of cardioplegic arrest [2–6, 8]. The ability of blood to deliver oxygen is an important characteristic contributing to its documented superiority over crystalloid cardioplegia in functional recovery and preservation of ultrastructure. Preservation of aerobic metabolism, decreased lactic acid buildup, and maintenance of high-energy phosphate levels during hypothermic arrest with blood cardioplegia have been demonstrated [3]. In addition to its ability to deliver oxygen, blood contains glucose, amino acids, natural buffers, free radical scavengers, and other metabolic substrates that enhance its efficacy as a cardioplegic agent.

However, hemoglobin's sigmoid-shaped oxygen dissociation curve shifts leftward under hypothermic conditions, restricting its ability to release oxygen at low temperatures [31, 32]. Blood also contains potentially injurious elements, such as leukocytes, platelets, and complement,

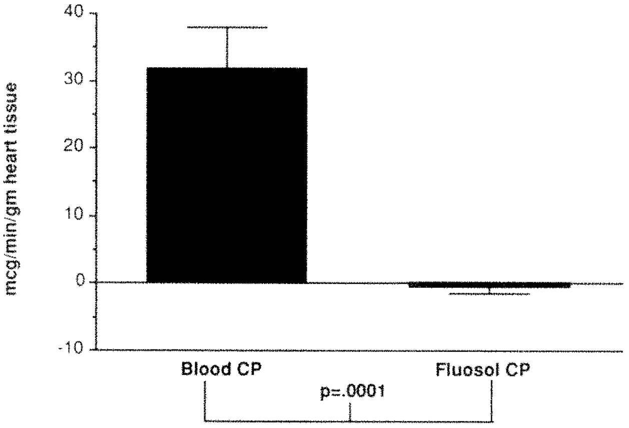


Fig 7. Lactate consumption 5 minutes after reperfusion was significantly greater (p = 0.0001) in blood cardioplegia (CP)–protected hearts than in those protected with Fluosol.

that may limit complete functional recovery. Leukocyte activation may occur with the initial dose of blood cardioplegia when preoperative ischemia or hypoxia exists, a form of reperfusion, as well as during repeated cardioplegia administration. Activated leukocytes have been documented to cause myocardial injury by a number of biochemical mechanisms including the production of oxygen-derived free radicals.

Fluosol is an acellular solution with the ability to bind and release oxygen in a linear fashion. Its oxygen-binding emulsion has a particle size of 0.1 to 0.2 μm, and its viscosity is lower than that of blood [15]. These characteristics may permit it to reach areas beyond critical stenoses and to perfuse the endocardium more readily than blood cardioplegia. The lack of cellular components and reactive blood proteins, such as fibrin and complement, may prevent capillary shutdown during both induction and repeated doses of cardioplegia, resulting in a more homogeneous distribution of cardioplegia and more complete protection.

Fluosol has a high affinity for oxygen and releases oxygen in a linear fashion unaffected by temperature [22, 33]. Despite a maximum oxygen content of 6 vol/100 mL versus 12 to 15 vol/100 mL for blood, the ability of Fluosol to release oxygen even at low temperatures results in greater oxygen uptake by the myocardium [33, 34]. The actual amount of oxygen required to maintain baseline aerobic metabolism in a hypothermically arrested heart is small, however, and our results indicate that both solutions provide sufficient amounts of oxygen to permit full functional recovery.

In this study, we demonstrated complete (94% to 100%) functional recovery with Fluosol cardioplegia and nearly complete recovery (89% to 95%) with blood cardioplegia. In previous studies [35] in our laboratory with crystalloid cardioplegia or hypothermia alone, complete functional recovery was not obtained. Therefore, the improved functional recovery seen with blood or Fluosol cardioplegia in the current study is due to improved protection by the solutions themselves and not to hypothermia alone.

Lactate consumption 5 minutes after reperfusion was significantly greater in the blood cardioplegia–protected hearts than in the Fluosol group and was similar to prearrest values. This difference may indicate earlier metabolic recovery in hearts protected with blood cardioplegia. However, lactate levels were not measured past 5 minutes of reperfusion, and hence the time course for recovery of this particular metabolic pathway in Fluosol-protected hearts is unclear. Others [4], however, have demonstrated that despite earlier return of net lactate consumption with blood cardioplegia than with crystalloid cardioplegia, lactate consumption normalized in both groups by 20 minutes of reperfusion. Despite the differences in early lactate metabolism in our study, high-energy phosphate levels were not significantly different between the two groups 1 hour after reperfusion. In addition, functional recovery was not affected by these early metabolic differences. Perhaps when preoperative energy depletion is present as under conditions of hypoxia and ischemia, the earlier metabolic recovery obtained with blood cardioplegia may be of importance. The addition of other metabolic substrates, such as monosodium glutamate and aspartate monohydrate, may improve the metabolic support afforded by Fluosol cardioplegia.

After initially promising results with Fluosol as a cardioplegic agent 7 to 10 years ago, preclinical and clinical trials were not carried out. The reason was twofold: (1) a clear advantage over blood cardioplegia was not consistently demonstrated, and (2) it was not approved for use by the Food and Drug Administration (FDA). Variations in calcium, sodium, and glucose concentration and in osmolarity between Fluosol, blood, and crystalloid cardioplegias in these early studies [36, 37] led to inconsistent findings, and the studies were inconclusive. Novick and associates [38] demonstrated 80% recovery of contractility in hearts protected with Fluosol versus only 50% recovery in hearts protected with blood cardioplegia. However, the calcium content of the Fluosol cardioplegia was twice that of the blood cardioplegia in this older study. To accurately compare Fluosol with blood cardioplegia, a calcium level of 1.1 mmol/L was maintained in both solutions in the present study.

After the FDA approved Fluosol in 1989 as a reperfusate during coronary angioplasty, interest in Fluosol as a cardioplegic agent was renewed. Initial concerns over its safety have been for the most part dismissed. There is no evidence in previous studies [36, 37], or in this study, that Fluosol increases myocardial edema, causes ultrastructural injury, or causes deposits in the myocardium.

Our results demonstrate complete functional recovery after 2 hours of cold ischemic arrest with Fluosol cardioplegia. Although the difference did not reach significance, hearts protected with Fluosol cardioplegia had slightly better functional recovery than blood cardioplegia–protected hearts (see Figs 3, 4). Previous studies comparing Fluosol cardioplegia with blood cardioplegia showed that although Fluosol did not lead to 100% recovery, it did provide protection equal to or better than that of blood cardioplegia.

Conclusion

Our data clearly demonstrate the ability of Fluosol to provide complete myocardial protection with 100% functional recovery after 2 hours of cold ischemic arrest in a normal unstressed heart. Despite no clear advantage over standard normocalcemic blood cardioplegia in this model, Fluosol's lack of cellular and acellular components may prevent reperfusion-associated injury, allowing superior myocardial protection when preoperative ischemia or hypoxia is present. Further studies using an ischemic model are necessary to fully evaluate the efficacy of Fluosol as a cardioplegic agent and its possible advantage over blood cardioplegia.

References

1. Williams WG, Rebeyka IM, Tibshirani RJ, et al. Warm induction blood cardioplegia in the infant. A technique to avoid rapid cooling myocardial contracture. J Thorac Cardiovasc Surg 1990;100:896–901.

2. Follette DM, Mulder DG, Maloney JV, Buckberg GD. Advantages of blood cardioplegia over continuous coronary perfusion or intermittent ischemia. Experimental and clinical study. J Thorac Cardiovasc Surg 1978;76:604–19.
3. Engelman RM, Rousou JH, Dobbs W, Pels MA, Longo F. The superiority of blood cardioplegia in myocardial preservation. Circulation 1980;62(Suppl 1):62–6.
4. Fremes SE, Christakis GT, Weisel RD, et al. A clinical trial of blood and crystalloid cardioplegia. J Thorac Cardiovasc Surg 1984;88:726–41.
5. Coetzee A, Roussouw G, Fourie P, Lochner A. Preservation of myocardial function and biochemistry after blood and oxygenated crystalloid cardioplegia during cardiac arrest. Ann Thorac Surg 1990;50:230–7.
6. Feindel CM, Tait GA, Wilson GJ, Klement P, MacGregor DC. Multidose blood versus crystalloid cardioplegia. Comparison by quantitative assessment of irreversible myocardial injury. J Thorac Cardiovasc Surg 1984;87:585–95.
7. Shapira N, Kirsh M, Jochim K, Behrendt DM. Comparison of the effect of blood cardioplegia to crystalloid cardioplegia on myocardial contractility in man. J Thorac Cardiovasc Surg 1980;80:647–55.
8. Catinella FP, Cunningham JN Jr, Knopp EA, Laschinger JC, Spencer FC. Preservation of myocardial ATP. Comparison of blood vs crystalloid cardioplegia. Chest 1983;83:650–4.
9. Hernandez LA, Grisham MB, Beverleigh T, Arfors KE, Harlan JM, Granger DN. Role of neutrophils in ischemia-reperfusion–induced microvascular injury. Am J Physiol 1987;253(Heart Circ Physiol 22):H699–703.
10. Go L, Murry CE, Richard VJ, Weischedel GR, Jennings RB, Reimer KA. Myocardial neutrophil accumulation during reperfusion after reversible or irreversible ischemic injury. Am J Physiol 1988;24(Heart Circ Physiol):H1188–98.
11. Breda MA, Drinkwater DC, Laks H, et al. Prevention of reperfusion injury in the neonatal heart with leukocyte-depleted blood. J Thorac Cardiovasc Surg 1989;97:654–65.
12. Stein DG, Permut LC, Drinkwater DC, et al. Complete functional recovery after 24 hour heart preservation with University of Wisconsin solution and modified reperfusion. Circulation 1991;84(Suppl 3):316–23.
13. Westlin W, Mullane KM. Alleviation of myocardial stunning by leukocyte and platelet depletion. Circulation 1989;80: 1828–36.
14. Litt MR, Richmond WJ, Weisman HF, Winkelstein JA, Becker LC. Neutrophil depletion limited to reperfusion reduces myocardial infarct size after 90 minutes of ischemia. Circulation 1989;80:1816–27.
15. Tokioka H, Miyazaki A, Fung P, et al. Effects of intracoronary infusion of arterial blood or Fluosol-DA 20% on regional myocardial metabolism and function during brief coronary artery occlusions. Circulation 1987;75:473–81.
16. Glogar DH, Kloner RA, Muller J, DeBoer LWV, Braunwald E, Clark LC Jr. Fluorocarbons reduce myocardial ischemic damage after coronary occlusion. Science 1981;211:1439–41.
17. Forman MB, Bingham S, Kopelman HA, et al. Reduction of infarct size with intracoronary perfluorochemical in a canine preparation of reperfusion. Circulation 1985;71:1060–8.
18. Kolodgie FD, Dawson AK, Roden DM, Forman MB, Virmani R. Effect of Fluosol-DA on infarct morphology and vulnerability to ventricular arrhythmia. Am Heart J 1986;112:1192–1201.
19. Cleman M, Jaffee CC, Wohlgelernter D. Prevention of ischemia during percutaneous transluminal coronary angioplasty by transcatheter infusion of oxygenated Fluosol DA 20%. Circulation 1986;74:555–62.
20. Anderson HV, Leimgruber PP, Roubin GS, Nelson DL, Gruentzig AR. Distal coronary artery perfusion during percutaneous transluminal coronary angioplasty. Am Heart J 1985;110:720–6.
21. Kent KM, Cleman MW, Cowley MJ, et al. Reduction of myocardial ischemia during percutaneous transluminal coronary angioplasty with oxygenated Fluosol. Am J Cardiol 1990;66:279–84.
22. Virmani R, Kolodgie FD, Osmialowski A, Zimmerman P, Mergner W, Forman MB. Myocardial protection by perfluorochemical infusion during transient ischemia produced by balloon coronary occlusion. Am Heart J 1988;116:421–31.
23. Naito R, Yokoyama K. Perfluorochemical blood substitutes: "FC-43 emulsion" "Fluosol-DA, 20% and 35%." Technical Information Series No. 5 1978:10–3.
24. Lowry OH, Passonneau JV. A flexible system of enzymatic analysis. New York: Academic Press, 1972:151–3.
25. Pridjian AK, Levitsky S, Krukenkamp I, Silverman NA, Feinberg H. Developmental changes in reperfusion injury. A comparison of intracellular cation accumulation in the newborn, neonatal, and adult heart. J Thorac Cardiovasc Surg 1987;93:428–33.
26. Nishioka K, Jarmakani JM. Effect of ischemia on mechanical function and high energy phosphates in rabbit myocardium. Am J Physiol 1982;242:H1077–83.
27. Grice WN, Konishi T, Apstein CS. Resistance of neonatal myocardium to injury during normothermic and hypothermic ischemic arrest and reperfusion. Circulation 1987; 76(Suppl 5):150.
28. Fujiwara T, Kurtts T, Anderson W, Heinle J, Mayer JE Jr. Myocardial protection in cyanotic neonatal lambs. J Thorac Cardiovasc Surg 1988;96:700–10.
29. Burrows FA, Williams WG, Teoh KH, et al. Myocardial performance after repair of congenital cardiac defects in infants and children. J Thorac Cardiovasc Surg 1988;96: 548–56.
30. Opie JC, Taylor G, Ashmore PG, Kalousek D. "Stone heart" in the neonate. J Thorac Cardiovasc Surg 1981;81:459–63.
31. Bull C, Stark J. Cardioplegia in pediatric cardiac surgery: repair in the first year of life. In: Engelman RM, Levitsky S, eds. A textbook of clinical cardioplegia. Mt. Kisco, NY: Futura, 1982:349–63.
32. Bull C, Cooper J, Stark J. Cardioplegic protection of the child's heart. J Thorac Cardiovasc Surg 1984;88:287–93.
33. Kirklin JK, Blackstone EH, Kirklin JW, McKay R, Pacifico AD, Bargeron LM. Intracardiac surgery in infants under age 3 months: incremental risk factors for hospital mortality. Am J Cardiol 1981;48:500–6.
34. Severinghaus JW. Oxyhemoglobin dissociation curve correction for temperature and pH variation in human blood. J Appl Physiol 1958;12:485–91.
35. Corno AF, Bethencourt DM, Laks H, et al. Myocardial protection in the neonatal heart. A comparison of topical hypothermia and crystalloid and blood cardioplegia solutions. J Thorac Cardiovasc Surg 1987;93:163–72.
36. Kanter KR, Jaffin JH, Ehrlichman RJ, Flaherty JT, Gott VL, Gardner TJ. Superiority of perfluorocarbon cardioplegia over blood or crystalloid cardioplegia. Circulation 1981;64(Suppl 2):75–80.
37. Rousou JH, Dobbs WA, Engelman RM. Fluosol cardioplegia: a method of optimizing aerobic metabolism during arrest. Circulation 1982;66(Suppl 1):55–9.
38. Novick RJ, Stefaniszyn HJ, Michel RP, Burdon FD, Salerno TA. Protection of the hypertrophied pig myocardium. A comparison of crystalloid, blood, and Fluosol-DA cardioplegia during prolonged aortic clamping. J Thorac Cardiovasc Surg 1985;89:547–66.

Influence of β_1-Blockade on Myocardial Substrates Early After a Coronary Operation

Örjan Desslén, MD, Jan van der Linden, MD, Rolf Ekroth, MD,
Per-Olof Joachimsson, MD, Lars Nordgren, MD, Sven-Olov Nyström, MD,
Gunnar Ronquist, MD, and Hans Tydén, MD

Departments of Thoracic and Cardiovascular Surgery, Anesthesiology, Clinical Physiology, and Clinical Biochemistry, University Hospital, Uppsala, Sweden

A high adrenergic strain during reperfusion after ischemia impedes functional recovery. Conversely, adrenergic blockade may be beneficial during reperfusion. This study was undertaken to find out if early postoperative high-dose infusion of the selective β_1-blocking agent metoprolol tartrate has additional effects on metabolic variables related to myocardial energy supply/demand balance compared with those obtained with a late preoperative oral dose. The study included 21 male patients undergoing coronary bypass grafting. All patients received an oral dose of metoprolol before the operation. After the operation, patients were randomized to a control group or a group receiving intravenous infusion of metoprolol. Myocardial uptake of oxygen and substrates was determined before and during atrial pacing. Metoprolol reduced arterial concentrations of free fatty acids, reduced myocardial uptake of free fatty acids, and enhanced myocardial uptake of lactate. During paced tachycardia, the metoprolol concentration correlated negatively with myocardial uptake of free fatty acids ($r = -0.80$; $p < 0.001$) and positively with myocardial uptake of lactate ($r = 0.53$; $p < 0.05$). It is concluded that postoperative infusion of metoprolol induces myocardial metabolic changes compatible with an improved energy supply/demand balance.

(Ann Thorac Surg 1992;54:1151–8)

There is general agreement that β-blockade should be maintained into the perioperative period of coronary artery bypass grafting to avoid withdrawal rebound phenomena and to improve myocardial energy supply/demand balance. It is common routine to continue the medication until a few hours before the start of the operation, but it generally is not resumed until oral intake is again possible. It may be that this leads to inadequate β-blockade during the highly adrenergic early postoperative period [1] and that an infusion of the blocking agent may be required for optimal β-blockade [2]. This seems desirable, as myocardial recovery is impeded by high adrenergic activity [3].

The general purpose of this study was to find out if early postoperative high-dose infusion of the selective β_1-blocking agent metoprolol tartrate has additional effects on metabolic variables related to myocardial energy supply/demand balance compared with those obtained with a late preoperative oral dose. It is generally believed that β-blockers improve myocardial energy metabolism largely, or even totally, by reducing heart rate [4, 5]. Other mechanisms for metabolic improvement have been suggested [6–8] but have not been unequivocally verified. This controversy prompted us to include periods of atrial pacing to eliminate effects that might be secondary to heart rate reduction. A specific aim was to clarify whether metoprolol has beneficial effects for the heart that are *not* secondary to a reduction in heart rate.

Only patients with an uneventful postoperative course were included to avoid the need for inotropic and other pharmacological treatment that might have influenced the results. It was assumed that these patients had a large margin to myocardial supply/demand imbalance that might conceal true effects from the infusion, and it was anticipated that the impact of metoprolol on myocardial energy supply/demand balance would be more clearly discernible if the margin to imbalance was reduced by increasing the myocardial energy demand. This was accomplished by paced tachycardia to 130 beats/min.

Material and Methods

Patients

Patients selected for the study met the following criteria: they were male and middle aged, in New York Heart Association functional class III with an ejection fraction of less than or equal to 0.30, preoperatively were on a long-term regimen of the selective β_1-blocking agent metoprolol, and were undergoing elective coronary artery bypass grafting. Patients with valve dysfunction or metabolic disorders in addition to the coronary artery disease were not considered. Twenty-seven patients were originally included based on these criteria. However, 6 had to be excluded for the following reasons: need of inotropic support during weaning from bypass (1 patient), reoperation because of bleeding (1 patient), anaphylactic reaction, probably induced by transfused blood plasma (2

Accepted for publication March 31, 1992.

Address reprint requests to Dr Wesslén, Department of Thoracic and Cardiovascular Surgery, University Hospital, S-751 85 Uppsala, Sweden.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Summary of Patient Data[a,b]

Variable	Control Group (n = 10)	Treated Group (n = 11)
Age (y)	61 ± 2	59 ± 2
Body weight (kg)	82 ± 4	81 ± 2
Previous myocardial infarction (0/1/2)	5/2/3	6/4/1
NYHA functional class (IIIA/IIIB)	5/5	3/8
Ejection fraction	0.58 ± 0.04	0.55 ± 0.03
Metoprolol (daily dose) (mg)	100 ± 13	122 ± 16
Aortic cross-clamping (min)	58 ± 5	57 ± 3
Extracorporeal circulation (min)	108 ± 8	113 ± 5
Peripheral anastomoses	3.3 ± 0.2	3.2 ± 0.1
CK-MB 18 hours postoperative (μkat/L)	0.64 ± 0.22	0.96 ± 0.40

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] No significant intergroup differences were observed.

CK-MB = myocardial-specific isoenzyme of creatine kinase; NYHA = New York Heart Association.

patients), failure of the coronary sinus catheter (1 patient), and lost blood samples (1 patient). Pertinent data for the remaining 21 patients are given in Table 1.

Clinical Management

All patients were premedicated with morphine sulfate (0.15 mg/kg) and scopolamine hydrobromide (0.006 mg/kg). Anesthesia was induced with midazolam hydrochloride (0.1 mg/kg), fentanyl (30 μg/kg), and pancuronium bromide (0.1 mg/kg) and maintained with continuous infusion of midazolam (0.1 mg $\cdot$ kg^{-1} $\cdot$ h^{-1}) and fentanyl (15 μg $\cdot$ kg^{-1} $\cdot$ h^{-1}). The patients were ventilated with air and oxygen. The operations were performed with standard cardiopulmonary bypass using a bubble oxygenator (Bentley 10 PLUS; Baxter Healthcare Corporation, Santa Ana, CA), moderate hypothermia (30°C), and hemodilution (hematocrit, 0.20 to 0.25). Multidose St. Thomas' cardioplegia was used. Cardiopulmonary bypass was ended after rewarming to a rectal temperature of 36°C. Heparin sodium was neutralized with protamine chloride until the preoperative activated clotting time was achieved.

After transfer of the patient to the intensive care unit, radiant heat was provided by a thermal ceiling (OPN thermal ceiling; Aragona AB, Sweden) suspended over the bed. Postoperatively, during the study period, the patients were normoventilated and analgesia was achieved by a continuous infusion of fentanyl (3 μg $\cdot$ kg^{-1} $\cdot$ h^{-1}) to enhance hemodynamic stability. No glucose- or lactate-containing fluids were given before or during the study.

During the operation, epicardial pacemaker leads were attached to the right atrium close to the junction between the superior vena cava and the right atrium (but away from the sinus node).

Study Protocol

Measurements were performed at the following periods:

1. Before induction of anesthesia (before anesthesia)

Approximately 3 hours after the declamping of the aorta, when the patient was in the intensive care unit in hemodynamically stable condition, measurements were again obtained.

2. Stable sinus rhythm (basal postoperative state)
3. After 10 minutes of atrial pacing to 130 beats/min (pacing I)
4. 20 Minutes after sinus rhythm reestablished (before randomization)

After the fourth measurement, the patient was randomly allocated to either the intravenous metoprolol infusion group (treated group) or the control group. The treated group received metoprolol as a bolus injection of 0.1 mg/kg followed by an infusion of 0.04 mg $\cdot$ kg^{-1} $\cdot$ h^{-1} immediately after the termination of the fourth measurement.

5. 20 Minutes after the bolus injection in the treated group and at a corresponding time in the control group (after randomization)
6. After 10 minutes of atrial pacing to 130 beats/min (pacing II)

Measurements

HEMODYNAMICS VARIABLES. A Swan-Ganz thermodilution pulmonary artery catheter and a central venous catheter were inserted through the right internal jugular vein before induction of anesthesia. These catheters were used to measure central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, pulmonary artery temperature, and cardiac output by thermodilution technique. Arterial blood pressure was measured in the left radial artery.

CORONARY SINUS BLOOD FLOW. A coronary sinus catheter (Wilton Webster Lab, MA) was inserted under fluoroscopy from the right internal jugular vein before induction of anesthesia. Coronary sinus blood flow was estimated by retrograde, continuous thermodilution technique [9] with a constant infusion (40 mL/min) of saline solution at room temperature (pump model, SAGE 351; Sage Inc, MA).

BLOOD GASES. Samples in duplicate for oxygen saturation and hemoglobin content were measured using an OSM 2 Hemoximeter (Radiometer, Copenhagen, Denmark). Oxygen tension was measured using an ABL 2 blood gas analyzer (Radiometer). The blood oxygen content (mmol/L) was calculated according to the formula

$$[\mathrm{B} - \mathrm{Hb(g/L)} \cdot \mathrm{HbSo_2(\%)} \cdot (6.2 \cdot 10^{-4})] + [\mathrm{Po_2(kPa)} \cdot 0.01]$$

where B = blood, Hb = hemoglobin, So_2 = oxygen saturation, and Po_2 = oxygen tension.

The myocardial oxygen uptake (μmol/min) was calculated according to the formula

$$[\text{Arterial oxygen content } (\mu\text{mol/L}) - \text{coronary sinus oxygen content } (\mu\text{mol/L})] \cdot \text{coronary sinus blood flow (L/min)}$$

LABORATORY METHODS. Samples for blood glucose determination were obtained in triplicate and analyzed by the glucose oxidase method. Plasma lactate and pyruvate levels and serum glycerol levels were determined by employing auxiliary enzymes culminating in a redox reaction. This reaction involved lactate dehydrogenase monitoring the conversion of the coenzyme (NAD^+/NADH) at 340 nm with the adoption of a molecular extinction coefficient for NADH of 6,3 [$1 \cdot \text{mmol}^{-1} \cdot \text{cm}^{-1}$]. Free fatty acids (FFAs) in serum were assayed by an enzymatic procedure [10]. The myocardial uptake of substrates was calculated according to the formula

$$[\text{Arterial substrate content } (\mu\text{mol/L}) - \text{coronary sinus substrate content } (\mu\text{mol/L})] \cdot \text{coronary sinus blood (or plasma flow) (L/min)}$$

ELECTROCARDIOGRAPHIC RECORDINGS. Twelve-channel electrocardiographic tracings were obtained before and 5 days after the operation. The electrocardiographic criteria for a perioperative myocardial infarction included the origin of a new Q wave or, if the heart rate was unchanged, a new bundle-branch block [11].

CARDIAC ENZYMES. Blood samples were taken 18 hours after the operation for the myocardial-specific isoenzyme of creatine kinase (reference value, <0.6 μkat/L) and aspartate aminotransferase (reference value, <0.6 μkat/L) analyses. The enzymatic signs of a perioperative myocardial infarction were a serum level of the myocardial-specific isoenzyme of creatine kinase of greater than or equal to 2.0 μkat/L or an aspartate aminotransferase value of greater than or equal to 2.5 μkat/L.

METOPROLOL. Plasma metoprolol levels were assayed using a gas chromatographic method [12].

Statistical Methods

Randomization was performed by a computerized procedure of sequential allocation including the patient's age, weight, initial postoperative cardiac index, and initial postoperative pulmonary capillary wedge pressure [13]. Data are presented as the mean ± the standard error of the mean. Comparisons between the groups were performed using the Mann-Whitney U test for unpaired samples and the one-sample Wilcoxon signed rank test for testing against a standard value [14]. Standard linear regression analyses and the Spearman rank test were used. Multiple stepwise regression analyses were performed according to Draper and Smith [15]. The Marquardt-Levenberg method was used to obtain an exponential function with the best fit to the data. A p value of less than 0.05 was considered significant. The calculations were made with a computerized statistical package (RS/1; BBN Inc, MA).

Ethics

The study was done in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the University of Uppsala. Informed consent was given by the patients to participate in the study.

Results

The clinical course was uneventful with hemodynamic stability throughout the perioperative period. One patient in the metoprolol-treated group, however, sustained a perioperative myocardial infarction according to both electrocardiographic and enzymatic criteria. There was no hospital mortality.

Findings in Control Patients

In comparison with preoperative measurements, the major metabolic findings before the first pacing period were the lost myocardial uptake of FFAs despite increased arterial concentrations of FFAs and the more than halved fractional extraction of myocardial lactate. There were no differences between the study groups at this stage (Tables 2, 3). During the subsequent hours arterial concentrations of FFAs increased further in the control group, and myocardial uptake of FFAs was resumed and exceeded the preoperative value. A positive correlation was observed between arterial FFA levels and myocardial uptake of FFAs ($r = 0.75$; $p < 0.01$; pooled data from both groups). In contrast, myocardial uptake of lactate decreased during the same period in the control patients. The decreasing uptake of lactate corresponded to a decreasing fractional extraction of lactate (from 20% to 5% at the last measurement).

Atrial pacing increased heart rate from 90 to 130 beats/min and increased myocardial oxygen uptake by 27% ($p < 0.01$). This had no detectable effect on the myocardial uptake of substrates. Detailed data including pyruvate and glycerol measurements are given in Tables 2 and 3.

Findings in Metoprolol-Treated Patients

During the basal postoperative period the arterial levels of FFAs increased also in the treated group. The increase, however, was clearly less pronounced than in the control patients. In contrast to the control group, there was no detectable myocardial uptake of FFAs during the whole postoperative study period. The differences between the groups in arterial concentrations of FFAs and the corresponding myocardial uptake were evident before the intravenous infusion of metoprolol, and the difference in uptake was amplified during the infusion.

Myocardial lactate uptake was maintained in the treated group throughout the study in contrast to the findings in

Table 2. Arterial Concentrations of Substrates and Metoprolol Before and After Randomization to the Control Group and the Intravenous Metoprolol-Treated Group[a–d]

Variable	Group	Before Anesthesia	Basal Postoperative State	Pacing I	Before Randomization	After Randomization	Pacing II
Glucose (mmol/L)	Control	4.7 ± 0.3	5.4 ± 0.7	5.1 ± 0.5	5.2 ± 0.4	5.5 ± 0.5	5.3 ± 0.4
	Treated	NS	NS	NS	NS	NS	NS
		4.8 ± 0.2	4.9 ± 0.2	4.8 ± 0.1	4.9 ± 0.2	4.9 ± 0.1	5.1 ± 0.1
Lactate (mmol/L)	Control	1.0 ± 0.1	1.6 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.8 ± 0.2	1.6 ± 0.1
	Treated	NS	NS	NS	NS	NS	NS
		1.2 ± 0.1	1.7 ± 0.1	1.9 ± 0.2	2.0 ± 0.3	2.1 ± 0.4	2.0 ± 0.3
Pyruvate (μmol/L)	Control	49 ± 4	75 ± 10	80 ± 12	88 ± 13	99 ± 14	102 ± 15
	Treated	NS	NS	NS	NS	NS	NS
		58 ± 10	76 ± 10	81 ± 11	84 ± 10	90 ± 9	106 ± 10
FFAs (μmol/L)	Control	349 ± 42	605 ± 110	838 ± 91	856 ± 79	914 ± 109	825 ± 120
	Treated	NS	NS	$p < 0.01$	$p < 0.01$	NS	NS
		424 ± 53	415 ± 31	485 ± 48	565 ± 51	624 ± 75	669 ± 79
Glycerol (μmol/L)	Control	90 ± 16	166 ± 37	223 ± 23	214 ± 31	204 ± 24	179 ± 21
	Treated	NS	NS	NS	NS	NS	NS
		123 ± 28	152 ± 16	200 ± 19	226 ± 20	238 ± 25	247 ± 30
Metoprolol (nmol/L)	Control	146 ± 46	. . .	45 ± 17	. . .	. . .	41 ± 17
	Treated	NS		NS			$p < 0.01$
		319 ± 120		136 ± 54			274 ± 56

[a] Data are shown as the mean ± the standard error of the mean. [b] Comparisons were done using the Mann-Whitney U test for unpaired samples. [c] Statistical results are for intergroup differences. [d] For discussion of time periods, see Study Protocol section.

FFAs = free fatty acids; NS = not significant ($p \geq 0.05$).

the control group. As shown in Table 3, this difference was observed before the intravenous infusion of metoprolol and was amplified during the infusion. The pacing procedure increased myocardial oxygen uptake in the treated group equally at both periods, and the increase was equal to that in the control patients. Further data are given in Tables 2 and 3.

Relationship Between Plasma Concentrations of Metoprolol and Metabolic Variables

The metoprolol concentrations tended to be higher in the intravenous metoprolol-treated group before the infusion was started. The difference between the groups, as intended, was markedly amplified by the infusion. Regression analyses were performed in all patients individually using all consecutive measurements of metoprolol concentrations versus metabolic variables (including measurements before and during the intravenous infusion period). All individual correlation coefficients were tested for significance against zero. A significant correlation was found between metoprolol concentrations and arterial FFAs (mean $r_S = -0.42 \pm 0.13$; $p < 0.01$; 95% confidence interval, $-0.68 < \text{mean} < -0.15$) and between metoprolol concentrations and myocardial uptake of lactate (mean $r_S = 0.30 \pm 0.13$; $p < 0.05$; confidence interval, $0.04 < \text{mean} < 0.56$). The relationship between metoprolol and myocardial uptake of FFAs ($r = -0.17$) was not significant ($p = 0.22$).

Analysis of the relationship between metoprolol and plasma concentrations of FFAs during the first pacing period (before the infusion of metoprolol) indicated a significant negative correlation between the variables ($r = -0.45$; $p < 0.05$) (Fig 1). The arterial concentration of FFAs at the same measurement correlated with the myocardial uptake of FFAs ($r = 0.75$; $p < 0.01$), but no significant correlation was found between metoprolol concentrations at this stage and myocardial uptake of FFAs.

During the second pacing period (during intravenous infusion of metoprolol in the treated group), a negative correlation was found between plasma metoprolol concentration and arterial–coronary sinus difference in FFAs (Fig 2). Multiple stepwise regression analyses indicated that the variation in arterial–coronary sinus difference in FFAs was best explained by metoprolol ($r^2 = 0.64$; $p < 0.001$). The partial correlation for plasma concentration of metoprolol was -0.80 ($p < 0.01$) and for arterial FFAs, 0.47 ($p < 0.05$). Including myocardial oxygen uptake, arterial concentration of FFAs, or arterial–coronary sinus difference in lactate did not improve the model.

During the second pacing period, a positive correlation was observed between plasma metoprolol concentration and arterial–coronary sinus difference in lactate (Fig 3). Multiple stepwise regression analyses indicated that the variation in arterial–coronary sinus difference in lactate during pacing was best explained by a model that included metoprolol and arterial concentrations of lactate ($r^2 = 0.44$; $p < 0.01$). The partial correlation for plasma concentration of metoprolol was 0.53 ($p < 0.05$) and for arterial lactate, 0.54 ($p < 0.05$). Including myocardial oxygen uptake or arterial–coronary sinus difference in FFAs did not improve the model.

Table 3. Myocardial Uptake of Substrates Before and After Randomization to the Control Group and the Intravenous Metoprolol-Treated Group[a–d]

Variable	Group	Before Anesthesia	Basal Postoperative State	Pacing I	Before Randomization	After Randomization	Pacing II
Glucose (μmol/min)	Control	-0.1 ± 7.9^{e}	4.4 ± 7.0^{e}	4.4 ± 19.0^{e}	8.9 ± 8.6^{e}	15.4 ± 12.9^{e}	4.0 ± 14.3^{e}
	Treated	NS	NS	NS	NS	NS	NS
		8.5 ± 13.6^{e}	-1.6 ± 12.9^{e}	-5.4 ± 17.1^{e}	-5.9 ± 14.6^{e}	-15.9 ± 12.0^{e}	-5.2 ± 11.8^{e}
Lactate (μmol/min)	Control	25 ± 4^{f}	25 ± 7^{f}	18 ± 10^{e}	17 ± 7^{g}	15 ± 7^{e}	4 ± 6^{e}
	Treated	NS	NS	NS	NS	NS	$p < 0.05$
		38 ± 10^{f}	27 ± 5^{f}	42 ± 8^{f}	29 ± 5^{f}	24 ± 8^{f}	35 ± 10^{f}
$\text{Lactate}_{\text{frac}}$(%)	Control	48 ± 5^{f}	20 ± 6^{g}	13 ± 6^{e}	14 ± 5^{g}	11 ± 5^{e}	5 ± 5^{e}
	Treated	NS	NS	NS	NS	NS	NS
		43 ± 4^{f}	20 ± 4^{f}	22 ± 3^{f}	20 ± 4^{f}	14 ± 4^{f}	17 ± 3^{f}
Pyruvate (μmol/min)	Control	0.5 ± 0.6^{e}	0.8 ± 0.7^{e}	1.3 ± 0.5^{g}	1.7 ± 0.8^{g}	2.2 ± 0.6^{g}	1.3 ± 1.3^{e}
	Treated	NS	NS	NS	NS	NS	NS
		2.1 ± 0.8^{f}	1.4 ± 0.8^{e}	1.3 ± 1.1^{e}	1.6 ± 0.9^{e}	1.3 ± 0.7^{g}	2.5 ± 0.9^{g}
FFAs (μmol/min)	Control	4.6 ± 1.3^{g}	5.0 ± 3.1^{e}	12.5 ± 4.4^{g}	13.7 ± 3.8^{g}	16.1 ± 3.0^{f}	12.1 ± 2.0^{f}
	Treated	NS	NS	$p < 0.05$	$p < 0.05$	$p < 0.01$	$p < 0.01$
		7.2 ± 3.0^{f}	3.3 ± 1.6^{e}	2.9 ± 2.5^{e}	1.1 ± 2.8^{e}	-0.9 ± 2.8^{e}	-1.3 ± 3.8^{e}
Glycerol (μmol/min)	Control	0.6 ± 1.2^{e}	-6.0 ± 9.8^{e}	2.5 ± 2.0^{e}	1.4 ± 2.9^{e}	2.8 ± 2.1^{e}	2.2 ± 2.3^{e}
	Treated	NS	NS	NS	NS	NS	NS
		1.1 ± 1.5^{e}	0.7 ± 2.0^{e}	1.0 ± 1.9^{e}	-0.6 ± 2.2^{e}	0.7 ± 2.5^{e}	1.2 ± 3.9^{e}
Oxygen (μmol/min)	Control	448 ± 71^{f}	403 ± 43^{f}	508 ± 57^{f}	437 ± 30^{f}	432 ± 30^{f}	492 ± 46^{f}
	Treated	NS	NS	NS	NS	NS	NS
		632 ± 144^{f}	430 ± 32^{f}	549 ± 50^{f}	480 ± 35^{f}	428 ± 33^{f}	502 ± 38^{f}
ScsO_2(%)	Control	41.8 ± 3.1	44.3 ± 1.6	39.9 ± 0.8	40.5 ± 1.7	42.6 ± 1.6	42.6 ± 1.0
	Treated	NS	NS	NS	NS	NS	NS
		39.2 ± 2.1	41.6 ± 1.0	39.1 ± 1.3	39.1 ± 1.1	40.1 ± 1.3	39.6 ± 1.5
CS flow (mL/min)	Control	88 ± 12	107 ± 12	123 ± 13	106 ± 8	111 ± 9	134 ± 13
	Treated	NS	NS	NS	$p < 0.05$	NS	NS
		123 ± 27	122 ± 10	153 ± 14	131 ± 10	116 ± 8	134 ± 7

[a] Data are shown as the mean ± the standard error of the mean. [b] Comparisons were done using the Mann-Whitney U test for unpaired samples. [c] Statistical results are for the uptake/release of substrates (superscripts) and intergroup differences. [d] For discussion of time periods see Study Protocol section. [e] significance: NS, $p \geq 0.05$. [f] significance: $p < 0.01$. [g] significance: $p < 0.05$.

CS flow = coronary sinus blood flow; FFAs = free fatty acids; $\text{Lactate}_{\text{frac}}$ = fractional extraction of lactate; NS = not significant; ScsO_2 = coronary sinus blood oxygen saturation.

Hemodynamic Variables

Hemodynamic data are presented in Table 4.

Comment

In this study β_1-blockade was used in the early postoperative period of coronary bypass grafting to enhance myocardial energy metabolism. It could be argued that a well-revascularized heart does not require anti-ischemic therapy. This may be true when the myocardium has recovered from an operation. However, from metabolic and hemodynamic standpoints, normalization will take at least 10 hours. Until then, myocardial energy metabolism is abnormal, with a reduced capacity to match energy demand. This suggests that measures that enhance the energy supply/demand balance may be of value.

The major findings of this study were that effects compatible with a more favorable myocardial energy metabolism were induced by β_1-blockade in the early hours after coronary artery bypass grafting and that these effects could be observed at a paced heart rate, ie, these effects were not secondary to a lowered heart rate. The effects were discernible after a preoperative oral dose, but postoperative high-dose infusion of the antagonist amplified the effects significantly.

Study Design

The primary aim of this study was to find out if infusion of metoprolol a few hours after operation would achieve effects in addition to those obtained with a late preoperative dose of the β_1-blocking agent. Metoprolol was infused in a dose that was calculated to achieve plasma concentrations twice as high as normally required for adequate blockade. In other words, two groups both treated with metoprolol were compared. A wide variation in plasma concentrations of the blocking agent was found within each group, probably reflecting the large interindividual variation in elimination rate of metoprolol [16]. In fact, overlapping metoprolol concentrations were found between the groups. No doubt, it would have been easier

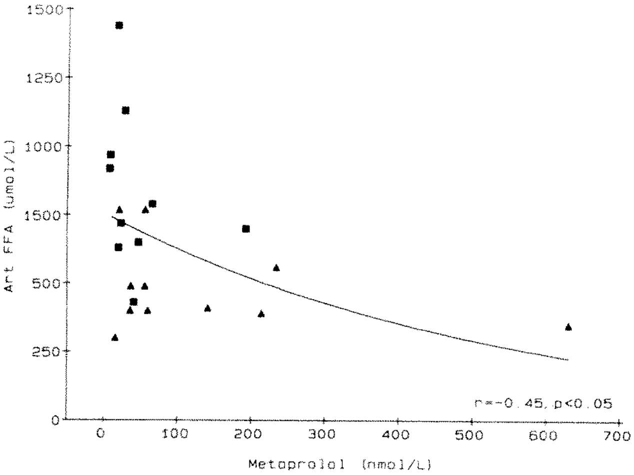


*Fig 1. Plasma concentration of metoprolol and arterial concentration of free fatty acids (*Art FFA*) during atrial pacing to 130 beats/min before metoprolol infusion. Ten patients were randomized to the control group (*squares*) and 11 patients to the intravenous metoprolol-treated group (*triangles*). The Marquardt-Levenberg method was used (see Statistical Methods section).*

to evaluate the effects of metoprolol if the patients in the control group had received no metoprolol at all. With the specific question in mind, and appreciating that preoperative withdrawal of the antagonist would have been ethically unpermissible [17], the difficulty seems inevitable. As a consequence of the study design, the risk for type II errors is imminent for comparisons between study groups. To compensate for this weakness in the study design, metoprolol concentrations, reflecting β-blocking activity at the receptor site, were measured and were related to hemodynamic and metabolic variables in regression analysis. We maintain that it is more adequate to analyze data in relation to actual metoprolol activity than in relation to the study group.

Along with these considerations were the higher metoprolol concentrations in the treated group before the infusion was started despite the fact the two groups had received a similar preoperative dose. Although the difference between the groups did not reach significance, it conceivably explains the difference in arterial FFA levels before the metoprolol infusion, as indicated by regression analyses, and also the difference in myocardial uptake of FFAs before the infusion.

The difference in lactate uptake between the study groups, already noted before the intravenous infusion of metoprolol, was also, according to regression analysis, the result of differences in metoprolol levels before the infusion was started.

Effects of Metoprolol

One reason for maintaining effective β_1-blockade in the early postoperative period is to avoid energy-consuming increases in heart rate. Previous work has shown that β_1-blockade may be of importance not only because it reduces heart rate, but also because it influences the myocardial uptake of substrates. Thus, the uptake of FFAs can be reduced, possibly secondary to reduced plasma concentrations [8]. This effect was also observed in our patients, with an inverse relationship between serum metoprolol levels and arterial–coronary sinus difference in FFAs ($r = -0.80$). A low uptake of FFAs is desired, as a high load of FFAs may lead to the accumulation of toxic metabolites and to an oxygen-wasting effect [18]. Free fatty acid oxidation at high catecholamine levels may increase oxygen expenditure up to 40% compared with what is required for the oxidation of carbohydrates [19].

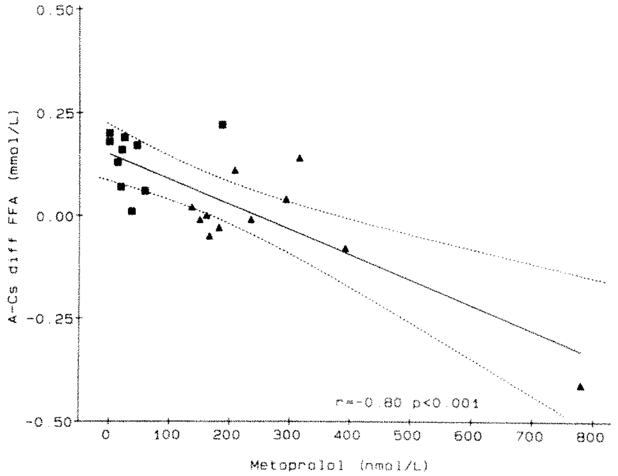


*Fig 2. Plasma concentration of metoprolol and myocardial arterial–coronary sinus difference in free fatty acids (*A-Cs diff FFA*) during atrial pacing to 130 beats/min and metoprolol infusion. There were 10 patients in the control group (*squares*) and 11 patients in the intravenous metoprolol-treated group (*triangles*). *Dashed lines* denote 95% confidence interval. Standard linear regression analysis was used.*

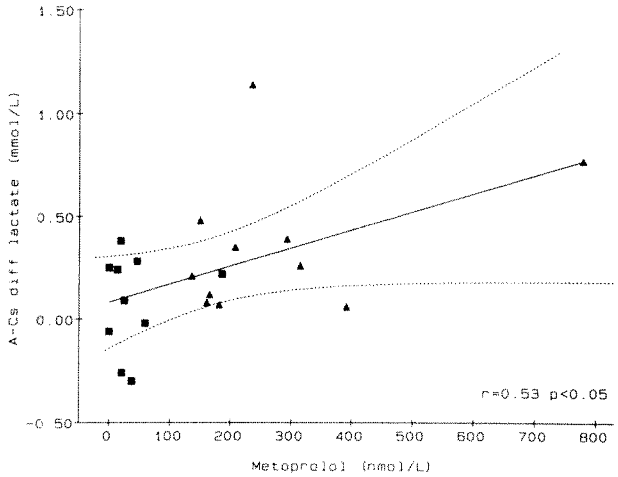


*Fig 3. Plasma concentration of metoprolol and arterial–coronary sinus difference in lactate (*A-Cs diff lactate*) during atrial pacing to 130 beats/min and metoprolol infusion. There were 10 patients in the control group (*squares*) and 11 patients in the intravenous metoprolol-treated group (*triangles*). *Dashed lines* denote 95% confidence interval. Standard linear regression analysis was used.*

Table 4. Hemodynamic Variables Before and After Randomization to the Control Group and the Intravenous Metoprolol-Treated Group[a–d]

Variable	Group	Before Anesthesia	Basal Postoperative State	Pacing I	Before Randomization	After Randomization	Pacing II
Temperature (°C)	Control	35.8 ± 0.1	36.3 ± 0.3	37.1 ± 0.3	37.6 ± 0.3	37.7 ± 0.4	38.0 ± 0.3
	Treated	NS	NS	NS	NS	NS	NS
		35.7 ± 0.1	36.2 ± 0.2	36.8 ± 0.3	37.3 ± 0.3	37.9 ± 0.3	38.2 ± 0.3
HR (beats/min)	Control	47 ± 2	88 ± 5	129 ± 1	103 ± 4	103 ± 5	129 ± 1
	Treated	NS	NS	NS	NS	NS	NS
		48 ± 2	90 ± 3	128 ± 1	98 ± 3	97 ± 2	128 ± 1
MAP (mm Hg)	Control	96 ± 7	76 ± 2	70 ± 3	70 ± 2	70 ± 3	68 ± 3
	Treated	NS	NS	NS	$p < 0.05$	NS	NS
		100 ± 5	81 ± 4	77 ± 3	78 ± 2	72 ± 2	71 ± 2
PCWP (mm Hg)	Control	12.0 ± 0.9	11.1 ± 1.1	12.1 ± 0.7	11.6 ± 0.8	11.8 ± 1.1	10.8 ± 0.7
	Treated	NS	NS	NS	NS	NS	NS
		13.9 ± 0.7	11.4 ± 0.7	14.2 ± 1.0	11.0 ± 0.8	11.1 ± 0.9	11.1 ± 0.6
CI ($L \cdot min^{-1} \cdot m^{-2}$)	Control	2.00 ± 0.19	2.50 ± 0.15	2.70 ± 0.19	2.87 ± 0.18	2.95 ± 0.13	2.89 ± 0.17
	Treated	NS	NS	NS	NS	NS	NS
		1.94 ± 0.12	2.41 ± 0.15	2.56 ± 0.12	2.73 ± 0.18	2.55 ± 0.16	2.56 ± 0.18
SI ($mL \cdot beat^{-1} \cdot m^{-2}$)	Control	42.4 ± 3.3	29.4 ± 2.3	21.0 ± 1.4	28.3 ± 2.3	29.3 ± 1.9	22.4 ± 1.3
	Treated	NS	NS	NS	NS	NS	NS
		40.1 ± 1.9	26.9 ± 1.6	20.1 ± 0.9	27.8 ± 1.6	26.2 ± 1.4	20.2 ± 1.3
SVR ($dynes \cdot sec \cdot cm^{-5}$)	Control	1,915 ± 200	1,107 ± 55	932 ± 88	907 ± 82	866 ± 80	872 ± 81
	Treated	NS	NS	NS	NS	NS	NS
		1,993 ± 166	1,294 ± 132	1,080 ± 81	1,058 ± 91	1,026 ± 86	995 ± 79
RPP (beats/min · mm Hg)	Control	6,821 ± 573	9,225 ± 575	12,741 ± 840	10,740 ± 762	10,489 ± 789	12,264 ± 594
	Treated	NS	NS	NS	NS	NS	NS
		7,383 ± 606	9,992 ± 465	13,245 ± 551	10,587 ± 478	9,730 ± 455	12,002 ± 423

[a] Data are shown as the mean ± the standard error of the mean. [b] Comparisons were done using the Mann-Whitney U test for unpaired samples. [c] Statistical results are for intergroup differences. [d] For discussion of time periods, see Study Protocol section.

CI = cardiac index; HR = heart rate; MAP = mean arterial pressure; NS = not significant; PCWP = pulmonary capillary wedge pressure; RPP = rate-pressure product; SI = stroke index; SVR = systemic vascular resistance; temperature = pulmonary artery temperature.

Again it may be argued that in a well-revascularized heart, the oxygen supply should not be rate-limiting. However, in the individual patient, the completeness of revascularization cannot be taken for granted, and also there is evidence that oxygen availability is reduced in the reperfusion period despite adequate blood flow [20].

High metoprolol concentrations were associated with a positive myocardial lactate uptake. This finding is in agreement with data from other clinical situations [6–8]. It is, however, at variance with data from other workers [4, 5], which indicated that the negative chronotropic effect of β-blockers was a prerequisite for myocardial metabolic effects. The discrepancy between those findings and the present data may be related to differences in sympathetic activity. The early postoperative period after a cardiac operation is highly adrenergic, whereas the sympathetic tone in the work by Schang and Pepine [4] and Simonsen and colleagues [5] probably was low, as judged from the relatively low heart rate before pacing. Pacing per se does not seem to increase the sympathetic tone [21]. It is thus suggested that β-blockade induces myocardial metabolic changes during pacing only when the sympathetic drive is increased.

The exact mechanism for the changed lactate uptake was not clarified by our data. At least three options are possible. First, improvement of the oxygen economy of the myocardium is possible, as the lactate conversion into acetylcoenzyme A implies the production of two stoichiometric units of NADH, whereas the corresponding acetylcoenzyme A from FFAs in β-oxidation yields only one NADH together with one $FADH_2$. The improvement of myocardial oxygen economy should reduce the stimulus for anaerobic glycolysis, with a reduced production of lactate and a higher gradient between extracellular and intracellular concentrations of lactate. This, in turn, would promote lactate uptake.

Second, an increased elimination of pyruvate, and secondary to this of lactate, is possible. The elimination of pyruvate is regulated by pyruvate dehydrogenase. The activity of this enzyme, in turn, is inhibited both by acetylcoenzyme A provided by β-oxidation and by hormones antagonistic to insulin, such as catecholamines. The β-blocker thus may increase the activity of the enzyme directly by blocking catecholamines and indirectly by reducing myocardial FFA metabolism and hence acetylcoenzyme A production.

Third, Nielsen and associates [7] suggested another mechanism for β-blockers to increase the elimination of lactate. They observed that propranolol increases the uptake of glutamate, which may be of importance both for the reduction of NADH and for the transamination of pyruvate to alanine.

The present data give no direct evidence of an improved oxygen economy from β_2-blockade during pacing, as the oxygen uptake was similar in the two groups. The reduced uptake of FFAs and the increased uptake of lactate suggest, however, that a more desirable metabolic situation was accomplished in terms of the oxygen economy of the heart.

Our findings are in keeping with pacing studies performed under nonsurgical conditions in patients with coronary artery disease [6–8]. Thus, similar effects were obtained regarding myocardial uptake of FFAs, lactate, and oxygen. Despite unchanged myocardial oxygen uptake during pacing tachycardia, the threshold to ischemic pain was increased in those patients.

Conclusion

The present data indicate that metoprolol, when infused to maintain adequate plasma concentrations in the early postoperative period of coronary bypass grafting, provides metabolic effects that are generally assumed to be beneficial to the myocardium in states with a poor energy metabolism. These effects contrasted with those observed in patients who had only a late preoperative dose. Furthermore, the study showed that β_1-blockade modifies myocardial metabolism at pacing; hence, β_1-blocking effects are not totally dependent on heart rate reduction.

The study was supported by grants from the Josef and Linnea Carlsson Foundation; the Gillberg Foundation; Hässle AB, Mölndal, Sweden; the Swedish Heart Lung Foundation; the University of Uppsala, Sweden; and the Zetterling Foundation.

Statistical advice was given by Anders Odén, PhD, Kungälv, Sweden.

References

1. Nilsson FN, Berglin W-O EE, Ekroth R, et al. Effects of graded insulin infusions on plasma levels of free fatty acids, adrenaline, and noradrenaline directly after open heart surgery. Thorac Cardiovasc Surg 1987;35:96–100.
2. Wesslén Ö, Ekroth R, Nyström S-O. An evaluation of the perioperative efficiacy of selective β_1-blockade in coronary surgery after a late preoperative dose of metoprolol. Studies with a late preoperative dose of metoprolol. Scand J Thorac Cardiovasc Surg 1989;23:151–4.
3. Kabas JS, Spratt JA, Davis JW, Rankin JS, Glower DD. The effects of dopamine on myocardial functional recovery after reversible ischemic injury. J Thorac Cardiovasc Surg 1990;100:715–23.
4. Schang SJ, Pepine CJ. Effects of propranolol on coronary hemodynamic and metabolic responses to tachycardia stress in patients with and without coronary disease. Cathet Cardiovasc Diagn 1977;3:47–57.
5. Simonsen S, Ihlen H, Kjekshus JK. Haemodynamic and metabolic effects of timolol (Blockadren®) on ischaemic myocardium. Acta Med Scand 1983;213:393–8.
6. Armstrong PW, Chiong MA, Parker JO. Effects of propranolol on the hemodynamic, coronary sinus blood flow and myocardial metabolic response to atrial pacing. Am J Cardiol 1977;40:83–9.
7. Nielsen TT, Bagger JP, Thomassen A. Improved myocardial lactate extraction after propranolol in coronary artery disease: effected by peripheral glutamate and free fatty acid metabolism. Br Heart J 1986;55:140–7.
8. Thompson DS, Naqvi N, Juul SM, Coltart DJ, Jenkins BS. Haemodynamic and metabolic effects of atenolol in patients with angina pectoris. Br Heart J 1980;43:668–79.
9. Ganz W, Tamura K, Marcus HS, Donoso R, Yoshida S, Swan HJC. Measurement of coronary sinus blood flow by continuous thermodilution in man. Circulation 1971;44:181–95.
10. Shimizu S, Yamada H. Free fatty acids: calorimetric method. In: Bergmeyer HU, ed. Methods of enzymatic analysis; vol 8. 3rd ed. Weinham, Germany: Verlag Chemie, 1985:19–25.
11. Goldman MJ. Principles of clinical electrocardiography. 12th ed. Los Altos, CA: Lange Medical, 1986.
12. Ervik M, Kylberg-Hanssen K, Johansson L. Determination of metoprolol in plasma and urine using high-resolution gas chromatography and electron-capture detection. J Chromatogr 1986;381:168–74.
13. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biomedics 1975;31:103–15.
14. Siegel S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill International, 1956.
15. Draper NR, Smith H. Applied regression analysis. New York: John Wiley, 1966.
16. Jordö L, Attman PO, Johansson L, Johnsson G, Regårdh CG. Pharmacokinetic and pharmacodynamic properties of metoprolol in patients with impaired renal function. Clin Pharmacokinet 1980;5:169–80.
17. Slogoff S, Keats AS, Ott E. Preoperative propranolol therapy and aortocoronary bypass operation. JAMA 1978;240:1487–90.
18. Vik-Mo H, Mjös OD. Influence of free fatty acids on myocardial oxygen consumption and ischemic injury. Am J Cardiol 1981;48:361–5.
19. Simonsen S, Kjekshus JK. The effect of free fatty acids on myocardial oxygen consumption during atrial pacing and catecholamine infusion in man. Circulation 1978;58:484–91.
20. Kanter KR, Glower DD, Schaff HV, Gardner TJ. Mechanism of defective oxygen extraction following global ischemia. J Surg Res 1981;30:482–8.
21. Dominiak P, Delius W, Grobecker H. Changes in plasma catecholamine concentrations in patients with coronary heart disease during pacing and physical exercise. Clin Cardiol 1985;8:77–81.

Pleuropulmonary Aspergilloma: Clinical Spectrum and Results of Surgical Treatment

Gilbert Massard, MD, Norbert Roeslin, MD, Jean-Marie Wihlm, MD,
Pascal Dumont, MD, Jean-Paul Witz, MD, and Georges Morand, MD

Department of Thoracic Surgery, University Hospital of Strasbourg, Strasbourg, France

From 1974 to 1991, 77 patients were admitted for pulmonary (55), pleural (16), or bronchial (6) aspergilloma. About 50% were asymptomatic. Sixty-three underwent operation. Pulmonary aspergillomas were operated on for therapeutic need in 26 and on principle in 18; the procedures were 28 lobar or segmental resections, 10 thoracoplasties, and 5 pleuropneumonectomies (1 patient had exploration only). Pleural aspergillosis was treated by operation on principle in 5 and for therapeutic need in 8 patients; 10 thoracoplasties, 1 attempt at pleuropneumonectomy, and 2 decortications were performed. All six bronchial lesions were operated on as a rule. Overall postoperative mortality was 9.5%. Major complications were bleeding (n = 37), pleural space problems (n = 24), respiratory failure (n = 6), and postpneumonectomy empyema (n = 4). All patients with pleural disease experienced complications. The outcome was better after lobar or segmental resection than after thoracoplasty (mortality, 6% versus 15%). Asymptomatic and nonsequellary pulmonary or bronchial aspergilloma also had an improved outcome. We conclude that operation is at low risk in pulmonary or bronchial locations in asymptomatic patients and in the absence of sequellae; the risk is high in symptomatic patients for whom operation is the only definite treatment. Pleuropneumonectomy should be avoided. Only symptomatic pleural aspergilloma should be operated on.

(Ann Thorac Surg 1992;54:1159–64)

Surgical decision-making for pulmonary or pleural aspergilloma is one of the major dilemmas shared by the chest physician and the thoracic surgeon. The former is unable, even with the most sophisticated investigations, to predict cataclysmic hemoptysis. The latter has the means of a definite cure; however, operation frequently is technically difficult, and postoperative outcome is known to have a high morbidity and mortality rate.

The purpose of our review was (1) to compare the different locations of aspergilloma (ie, pulmonary, pleural or bronchial), (2) to assess postoperative complications, and (3) to define high-risk and low-risk subgroups.

Material and Methods

Patients

We reviewed records of 77 patients admitted with pleuropulmonary aspergilloma from 1974 through 1991. There were 57 male and 20 female patients, with a mean age of 49 years (range, 16 to 75 years). Three groups were defined according to the location of the disease: pulmonary aspergilloma (55 patients), pleural aspergilloma (16 patients), and bronchial aspergilloma (6 patients).

Methods

The three groups of patients were compared with respect to mean age, nutritional status (percentage of the ideal weight estimated with the Lorentz formula), respiratory function (percentage of vital capacity and of forced expiratory volume in 1 second/forced vital capacity), and serodiagnosis (number of precipitations on immunoelectrophoresis). For each patient, we noted the underlying disease, the diagnostic circumstances, radiologic findings, and the reasons for surgical decision.

Postoperative outcome was assessed for mortality and major nonfatal complications (hemorrage, pleural space problems, and respiratory distress). A postoperative hospital stay exceeding 30 days was noted as an objective indicator of major complications. Bleeding was evaluated through the summed operative blood loss and postoperative drainage of the first 24 hours; we considered as major bleeding any quantity exceeding 1,500 mL. Pleural space problems included prolonged air leaks, secondary pneumothoraces, and postoperative aspergillus empyema. Respiratory failure was defined by the necessity of artificial ventilation beyond the first 24 hours.

The analysis was conducted considering first the location of aspergilloma and second the type of surgical procedure. A further comparative study was made on the basis of subgroups created within the operated pulmonary and bronchial aspergillomas (total = 50): operation on principle in asymptomatic patients (26) versus therapeutic need (24), and parenchymal sequelae (40) versus absence of underlying disease (10). These subgroups were compared for nutritional status, respiratory function, and postoperative outcome. Pleural aspergillosis was ex-

---

Accepted for publication April 6, 1992.

Address reprint requests to Dr Massard, Service de Chirurgie Thoracique, Hospices Civils, CHRU, F-67091 Strasbourg-Cedex, France.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. General Variables and Location of Aspergilloma[a]

Variable	Pulmonary (n = 55)	Pleural (n = 16)	Bronchial (n = 6)	Statistics	
				t Value	*p* Value
Age (y)	48.2 ± 14.2	54.6 ± 13.6	40.2 ± 17.4	2.07	<0.05
Nutrition[b]	86.2 ± 13.2	83.8 ± 12.1	111.8 ± 26.9	4.15	<0.001
VC[c]	77.5 ± 23.9	65.5 ± 16.2	97.5 ± 14.5	2.77	<0.01
FEV_1/VC[c]	60.4 ± 16.9	67.8 ± 14.1	78.3 ± 7.9	2.48	<0.05
Serodiagnosis[d]	6.3 ± 3.9	7.1 ± 3.3	2.6 ± 1.7	Not significant	

[a] Values are expressed as mean ± standard deviation. [b] Percentage of the "ideal weight" estimated with the Lorentz formula: ideal weight = height (cm) − 100 − (height (cm) − 150/a) with a = 4 for men and a = 2.5 for women. [c] Percentage of the theoretical values according to sex, age, height, and weight. [d] Number of precipitations on immunoelectrophoresis.

FEV_1 = forced expiratory volume in 1 second; VC = vital capacity.

cluded from this analysis because it is a quite different disease.

Statistical analysis was performed with Student's *t* test; a *p* value less than 5% was considered to be significant.

Results

Age, Nutritional Status, Respiratory Function, and Serodiagnosis

We noticed an obvious difference between bronchial aspergilloma on the one hand, and pulmonary or pleural aspergilloma on the other hand (Table 1). Bronchial aspergilloma occurred in younger patients ($t = 2.07$; $p < 0.05$), patients with a better nutritional status ($t = 4.15$; $p < 0.001$), and functionally less disabled patients ($t = 2.77$ and $p < 0.01$ for vital capacity; $t = 2.48$ and $p < 0.05$ for forced expiratory volume in 1 second/vital capacity). Positivity on immunoelectrophoresis was comparable for all types of aspergilloma.

Underlying Disease

The vast majority of pulmonary aspergillomas (80%) had developed in parenchymal cavitations, which were sequelae of tuberculosis in 35 patients and of a lung abcess in 9 patients. Another 7 had grown on pulmonary fibrosis secondary to radiation therapy (4 patients, 1 of whom had semiinvasive aspergillosis), sarcoidosis (2 patients) or lung infarction (1 patient). No underlying disease was noticed in 4 patients.

Bronchial aspergilloma appeared as bronchial mycetoma in 4 patients, as bronchocentric granuloma in 1 patient, and as Hinson's disease in 1.

Nearly all of the 16 pleural aspergillomas were located in a pleural space that was residual to lobectomy in 10 patients (6 lobectomies for cancer, 3 for tuberculosis, 1 for aspergilloma), to exploratory thoracotomy in 1, and to collapsotherapy in 3. The remaining 2 patients had spontaneous bronchopleural fistulas.

Clinical and Radiological Findings

Fifty-two percent of the pulmonary aspergillomas were symptomatic; the predominant symptom was hemoptysis in 13 patients, bronchorrhea in 7, and fever and weight loss in 8. Twenty-one aspergillomas were diagnosed by follow-up roentgenograms, and 6 were discovered while these patients were being investigated for an extrathoracic disease. Pleural aspergillomas were symptomatic in 7 patients (hemoptysis, sputum, pain); 6 were diagnosed on follow-up and 3 on check-up chest films. All 6 bronchial aspergillomas were seen as check-up findings in asymptomatic patients.

The most common radiologic finding with pulmonary locations was the air-crescent sign (42 patients). Another 8 patients had a cavitation, 3 a recent modification of sequelae, and 2 a pseudotumoral opacity. Pleural aspergilloma resulted in 10 thickenings of pleural sequelae and in 6 empyemas. Bronchial aspergilloma occurred as a pseudotumor in all 6 patients.

Therapeutic Decision

Fourteen patients were managed without operation. The reasons were age and bad general health for 5 patients, bilateral lesions and severe restrictive lung disease for 3 others, refusal by the patient for 3, relapsing generalized cancer for 1, decompensated cirrhosis for 1, and aspergilloma developed on the remaining lung after pneumonectomy for 1.

A surgical procedure was performed on 63 patients: 44 had pulmonary aspergilloma, 13 had a pleural location, and a further 6 had bronchial disease. For pulmonary aspergillomas, operation was decided on for reasons of therapeutic need in 26 patients (importance of the symptoms in 17, rapid growth on chest films in 7, and coexisting bronchogenic cancer in 2), whereas 18 asymptomatic patients were operated on on principle (14 to prevent later complications, 4 because of a lack of diagnosis). Pleural aspergillomas were indicated for operation on principle in 5 patients, after failure of a medical treatment in 3 others, because of disabling symptoms in 2, because of radiologic growth in 2, and to resect simultaneously bronchogenic cancer relapsing after left lower lobectomy in 1. All 6 patients with bronchial aspergillomas had no complaint and underwent thoracotomy to clear a diagnostic doubt.

Surgical Procedure

Pulmonary aspergilloma (n = 44) was mainly resected: 5 by segmentectomy, 23 by lobectomy, and 5 by pleuropneumonectomy. Ten other patients had removal of the

Table 2. Postoperative Outcome: Overall Results

Variable	Pulmonary (n = 44)	Pleural (n = 13)	Bronchial (n = 6)	Total (n = 63)
Mortality	4	2	0	6
Nonfatal complications	32	11	1	44
Hospital stay >30 days	21	9	1	31
Detailed nonfatal complications				
Hemorrhage	27	9	1	37
Pleural space problems	15	8	1	24
Respiratory failure	5	1		6
Empyema thoracis[a]	4			4
Lobar infarction[b]	1			1

[a] Empyema after pleuropneumonectomy. [b] Venous lobar infarction after right upper lobectomy.

mycetoma by pleuropneumotomy associated with immediate thoracoplasty. Thoracotomy was exploratory in 1 patient with coexisting bronchogenic cancer that proved to be unresectable.

Pleural aspergilloma (n = 13) was treated with first-choice thoracoplasty in 10 patients. Decortication performed on 2 patients was ineffective; both required secondary thoracoplasty. Pleuropneumonectomy was attempted on a patient with pleural aspergillosis and relapsing cancer after left lower lobectomy; fatal bleeding occurred during this procedure.

All bronchial aspergillomas (n = 6) were resected, either by segmentectomy (3) or by lobectomy (3).

Postoperative Mortality and Operation-Related Morbidity

Six patients died perioperatively (Table 2). One patient had fatal operative bleeding during a pleuropneumonectomy for pleural aspergilloma and relapsing cancer. Five deaths (4 pulmonary and 1 pleural aspergilloma) in the postoperative course were related to severe bronchopulmonary infections and respiratory failure.

Forty-four patients had 72 major complications; for 31, postoperative hospital stay exceeded 30 days. Important blood loss was noted in 37 patients (27 pulmonary, 9 pleural, and 1 bronchial aspergilloma).

Pleural space problems occurred in 24 patients; they occurred as prolonged air leaks in 7, as a residual pleural pocket in 15, and as *Aspergillus* empyema in 2. Management required 6 tube thoracostomies and 5 thoracoplasties. Most of these complications (n = 15) were seen after treatment of pulmonary aspergilloma; 8 were seen after treatment of pleural locations (3 persistent air leaks and 5 residual pockets), and 1 case of *Aspergillus* empyema occurred after resection of a bronchial mycetoma.

Six patients had respiratory distress, 4 of whom needed tracheotomy for long-term respiratory assistance. One of these patients had a pleural aspergilloma.

The remaining complications included 4 empyemas after pneumonectomy (all treated by lavage and second-choice thoracoplasty) and one venous infarction of the right lower lobe after right upper lobectomy requiring emergency reexploration for completion pneumonectomy.

Outcome Related to the Operative Procedure

Lobectomy or segmentectomy was performed on 34 patients (Table 3). Two patients died postoperatively (6%). Fifteen had major bleeding, 16 had space problems, and 1 had respiratory distress. Hospital stay exceeded 30 days for 11.

Twenty patients had pleuropneumotomy for removal of the mycetoma and immediate thoracoplasty. There were three postoperative deaths (15%). Important blood loss was noted in 17 patients, space problems in 6, and respiratory distress in 5. Hospital stay was beyond 30 days in 13.

Pleuropneumonectomy, which was attempted six times, caused one intraoperative death. All the 5 surviving patients had major bleeding, and 4 experienced empyema thoracis. These 4 had a prolonged hospital stay.

Subgroup Studies

Patients who underwent operation on principle had a significantly better nutritional status ($t = 3.22$; $p < 0.01$)

Table 3. Postoperative Outcome Related to the Surgical Procedure[a]

Variable	Lobectomy (n = 34)	Thoracoplasty (n = 20)	Pneumonectomy (n = 6)	Statistics	
				t Value	*p* Value
Mortality	2	3	1		
Hemorrhage	15	17	5		
Pleural space problems	16	6			
Empyema thoracis			4		
Respiratory distress	1	5			
Hospital stay >30 days	11	13	4		
Weight[b]	94.9 ± 17.8	79.3 ± 8.7	76.4 ± 8.2	2.75	<0.01
Vital capacity[c]	91 ± 17.9	56.6 ± 16.3	59.6 ± 21.6	3.63	<0.01

[a] Three patients are not included in this table: 2 underwent decortication and 1 had exploratory thoracotomy. [b] Percentage of the "ideal weight" estimated with the Lorentz formula: ideal weight = height (cm) − 100 − (height (cm) − 150/a) with a = 4 for men and a = 2.5 for women (mean ± standard deviation). [c] Percentage of the normal values for vital capacity according to sex, age, height, and weight (tables of the CECA) (mean ± standard deviation).

Table 4. Postoperative Outcome: Operation on Principle Versus Therapeutic Need

Variable	Operation on Principle (n = 24)	Symptomatic (n = 26)	Statistics	
			t Value	*p* Value
Mortality	0	4		
Hemorrhage	11	17		
Pleural space problems	8	8		
Respiratory failure	1	4		
Hospitalization >30 days	6	16		
Weight[c]	97.3 ± 19.1	82.9 ± 11.9	3.22	<0.01
Vital capacity[d]	91.9 ± 18	73.1 ± 24.3	3.02	<0.01

[a] To prevent complications (n = 14) or to clear a diagnostic doubt (n = 10). [b] Disabling symptoms (n = 15), rapid growth (n = 7), or coexisting cancer (n = 2). [c] Percentage of the "ideal weight" estimated with the Lorentz formula: ideal weight = height (cm) − 100 − (height (cm) − 150/a) with a = 4 for men and a = 2.5 for women (mean ± standard deviation). [d] Percentage of the normal values according to sex, age, height, and weight (tables of the CECA) (mean ± standard deviation).

and an improved vital capacity ($t = 3.02$; $p < 0.01$) than the patients with a therapeutic need. These findings are correlated with a better postoperative outcome (Table 4).

Comparing patients without any underlying disease with those having parenchymal sequelae allowed similar and even more obvious conclusions: nutritional status was improved in the former ($t = 3.33$; $p < 0.001$), as were vital capacity ($t = 2.37$; $p < 0.01$) and postoperative prognosis (Table 5).

Comment

Our personal series is comparable in number to the outstanding publications of Daly [1], Karas [2], Jewkes [3], and their associates. It differs in that 21% of our patients had pleural aspergilloma, which appears to be an important experience considering the rare publications relative to this location.

We observed improved nutritional status, respiratory function, and postoperative outcome in patients with bronchial aspergilloma, as compared with pulmonary or pleural locations. In both the latter groups, bad general health associated with pathologic or even operated or irradiated lungs favors *Aspergillus* infection and postoperative complications. On the contrary, a mycetoma growing in a bronchus of an otherwise healthy lung obviously is a more favorable disease. Daly and associates [1] came to the same conclusion when comparing "simple aspergilloma" (single lesion without sequelae) and "complex aspergilloma" (with pleural or parenchymal sequelae).

The pulmonary aspergillomas we observed agreed with the "European standard": most of them grew in metatuberculous cavitations, and the percentage remained in the same range we noted in a previous series [4]. On the other hand, North American series have less tuberculosis (33% reported by Faulkner and colleagues [5]), in place of which other causes are seen: histoplasmosis (29% in Faulkner and colleagues' series [5]), sarcoidosis, and association with ankylosing spondylitis [6]. When no cavitation is present, *Aspergillus* is able, through enzyme secretion, to dig into a lung that is disabled by lesions such as radiation pneumonitis, sarcoid fibrosis, and semi-invasive aspergillosis [7]. Pulmonary aspergillomas growing in healthy lungs are very similar to bronchial aspergilloma seen as bronchiectatic mycetoma. Besides, bronchial locations also include the bronchocentric granuloma and Hinson's disease, which is exceptionally of surgical interest. Pleural aspergillosis most often develops in a residual pleural space after operation (or formerly, after collapse therapy for tuberculosis) and is favored by a bronchopleural fistula [8].

Table 5. Postoperative Outcome: Existence of Sequelae Versus Absence of Underlying Disease

Variable	No Disease (n = 10)	Sequelae (n = 40)	Statistics	
			t Value	*p* Value
Mortality	0	4		
Hemorrhage	2	26		
Pleural space problems	2	14		
Respiratory distress	0	5		
Hospitalization >30 days	1	21		
Weight[a]	105.2 ± 24.6	85.8 ± 12.5	3.33	<0.001
Vital capacity[b]	97 ± 11.7	78.2 ± 24.1	2.37	<0.01

[a] Percentage of the "ideal weight" estimated with the Lorentz formula: ideal weight = height (cm) − 100 − (height (cm) − 150/a) with a = 4 for men and a = 2.5 for women (mean ± standard deviation). [b] Percentage of the normal values according to sex, age, height, and weight (tables of the CECA) (mean ± standard deviation).

Half of our patients (52%) were asymptomatic; this is in opposition to most of the published series. Excepting that of Jewkes and co-workers [2], 22% of whose patients were without symptoms, all major series are composed of symptomatic patients. This might be explained by our resolute surgical approach, mandated by the fear of evolutive complications.

Although computed tomographic scan is thought to be more efficient to diagnose incipient disease [9], we observed no advantage over the more classic tomograms.

Most of our patients (82%) had operative treatment, because they were referred by the department of chest medicine with a surgical decision. The literature provides series of very disparate origins, and we thus explain the percentage of patients undergoing operation varying from 26% to 100% [1, 5].

The main reason for operative treatment of aspergillomas is the important risk of evolving complications. Major hemoptysis is the most frequent accident and has been estimated to occur in 20% of the patients [3, 5]. Observed 5-year survival after hemoptysis was 84% for operated and 41% for nonoperated patients [3]; however, survival after minor hemoptysis (<150 mL) has been reported not to be improved by operation [5]. Besides, Rafferty and associates [10] observed development of invasive aspergillosis in 20% of their series, which might have been prevented by surgical excision. Although several authors reported spontaneous regression of the mycetoma, we did not find mention of a rapid growth, which was the main reason for operation in 7 of our patients.

There is no effective alternative to operation. Medical treatment, currently beneficial for invasive aspergillosis, has a questionable action on the megamycetoma. In our experience, only 4 patients with pulmonary aspergilloma had been treated with general antifungal therapy and were referred to our department after failure of this treatment. We believe that there is no indication for antifungals in the saprophytic *Aspergillus* infection. Direct intracavitary administration of antifungal agents should be reserved to inoperable subjects [11].

Surgical decision is difficult because the procedures are renowned to be technically hazardous and to have a complicated postoperative outcome. The observed mortality rate of 9.5% is to be compared with a range varying from 4.5% [12] to 44% [3] reported in the literature. In fact, the latter series is exclusively composed of acutely ill patients, whereas the former includes asymptomatic patients.

The most common incident is bleeding. Fifty percent of the patients in our series lost more than 1,500 mL during the operation and the following 24 hours; this is more than twice the blood loss after lobectomy for cancer. Personne and colleagues [12] relate that 75% of their patients needed blood transfusions of more than 2 L. Preoperative arterial embolization has been attempted to reduce operative bleeding [13]; it failed, as it did in a case of ours because the vascular network surrounding the mycetoma was irrigated by several pedicles.

Pleural space problems after lobectomy also are common and are a consequence of the loss of elasticity of the sequelar lung; preventive immediate thoracoplasty has been recommended and performed in up to 25% of the cases [12]. We prefer to do the thoracoplasty as a second-choice procedure after lobectomy, thus avoiding unnecessary mutilation to some patients: although 38% had reexpansion problems, only 12% required thoracoplasty. The problem is different in the case of pleural aspergilloma. Decortication failed twice: the underlying lung was too rigid to reexpand and to fill the pleural space. We believe that thoracoplasty is the most appropriate one-stage procedure; it should be large because 3 of our patients had a residual pouch after this procedure, requiring complementary rib resection in 1. Open-window thoracostomy has been reported as a successful procedure in 5 patients with *Aspergillus* empyema [14]. However, this procedure needs a second-stage operation after several weeks or months of local dressings, and most often muscle plombage is performed [14]. Unfortunately, in the particular case of pleural aspergilloma, the latissimus dorsi often has been cut during a previous thoracotomy; perhaps the functional result on the shoulder girdle after the transfer of the serratus or the pectoralis major is then no better than after a 4- or 5-rib thoracoplasty.

Respiratory failure is an inevitable complication in patients with disease-related restrictive lung disease.

Considering the type of procedure, it appears that all pleuropneumonectomies had a difficult postoperative course. We agree with Shirakusa and colleagues [14] in that this procedure should be avoided whenever possible. Outcome after thoracoplasty was worse than it was after lobar or segmental resection; we should point out that these patients were either functionally contraindicated for resection or had pleural disease (related with important parenchymal sequelae and disabled nutritional and functional status). Perhaps results might be improved overall if indications for resection were reduced in difficult cases, which could be treated at lower risk with pleuropneumotomy for removal of the mycetoma and immediate thoracoplasty. Furthermore, considering the important incidence of complications with pleural disease, operation should be limited to symptomatic patients in the pleural location.

Our subgroup analysis confirms the data of Daly and associates [1]: the operative risk is low in the absence of pleural or parenchymal sequelae. Operation on principle in asymptomatic patients also had a more favorable outcome in this series. This agrees with the findings that authors operating on only symptomatic patients relate a mortality rate of 38% [15] and even 44% [3]; when aspergilloma is operated on on principle, mortality approaches 7% [1].

In conclusion, effective treatment of pulmonary or pleural aspergilloma is necessarily surgical. The operative risk is very low in patients who are asymptomatic and have no sequelae, whereas the risk of evolving complications is real. Therefore, such patients should undergo operation on principle, the ideal procedure being segmental or lobar resection. In symptomatic patients, as well as in presence of pleural sequelae, the operative risk is high, especially when nutritional and functional status are bad.

However, operation is advised because the symptomatic manifestations may become life-threatening. A segmental or lobar resection may be attempted only if the lesions are confined to a single lobe, and if functional and nutritional status are consistent with a major surgical procedure. In all other events, a pleuropneumotomy for removal of the mycetoma followed by immediate thoracoplasty is the reasonable choice. In very debilitated patients, the alternative is intracavitary treatment. Operation on *Aspergillus* empyema is hazardous and should be limited to symptomatic patients; the most appropriate procedure in our experience is a generous thoracoplasty.

References

1. Daly RC, Pairolero PC, Piehler JM, Trastek VF, Payne WS, Bernatz PE. Pulmonary aspergilloma. Results of surgical treatment. J Thorac Cardiovasc Surg 1986;92:981–8.
2. Karas A, Hankins JR, Attar S, Miller JE, McLaughlin JS. Pulmonary aspergilloma: an analysis of 41 patients. Ann Thorac Surg 1976;22:1–7.
3. Jewkes J, Kay PH, Paneth M, Citron KM. Pulmonary aspergilloma: analysis of prognosis in relation to haemoptysis and survey of treatment. Thorax 1983;38:572–8.
4. Witz JP, Roeslin N, Morand G. Traitement chirurgical des aspergillomes pulmonaires et pleuraux. A propos de 57 observations. J Med Strasbourg 1977;8:767–71.
5. Faulkner SL, Vernon R, Brown PP, Fisher RD, Bender HW. Hemoptysis and pulmonary aspergilloma: operative versus nonoperative treatment. Ann Thorac Surg 1978;25:389–92.
6. Tomlinson JR, Sahn SA. Aspergilloma in sarcoid and tuberculosis. Chest 1987;92:505–8.
7. Kibbler CC, Milkins SR, Bhamra A, Spiteri MA, Noone P, Prentice HG. Apparent pulmonary mycetoma following invasive aspergillosis in neutropenic patients. Thorax 1988;43:108–12.
8. Krakowka P, Rowinska E, Halweg H. Infection of the pleura by *Aspergillus fumigatus*. Thorax 1970;25:245–53.
9. Roberts CM, Citron KM, Strickland B. Intrathoracic aspergilloma: role of CT in diagnosis and treatment. Radiology 1987;165:123–8.
10. Rafferty P, Biggs BA, Crompton GK, Grant IWB. What happens to patients with pulmonary aspergilloma? Thorax 1983;38:579–83.
11. Shapiro MJ, Albeda SM, Mayock RL, McLean GK. Severe hemoptysis associated with pulmonary aspergilloma. Percutaneous intracavitary treatment. Chest 1988;94:1225–31.
12. Personne C, Toty L, Colchen A, Hertzog P. Vrais et faux problèmes de la chirurgie des aspergillomes pulmonaires. A propos de 220 cas. Rev Fr Mal Resp 1979;7:43–4.
13. Hughes CF, Waugh R, Lindsay D. Surgery for pulmonary aspergilloma: preoperative embolization of the bronchial circulation. Thorax 1986;41:324–5.
14. Shirakusa T, Ueda H, Suito T, et al. Surgical treatment of pulmonary aspergilloma and *Aspergillus* empyema. Ann Thorac Surg 1989;48:779–82.
15. Henderson RD, Deslauriers J, Ritcey EL, Delarue NC, Pearson FG. Surgery in pulmonary aspergillosis. J Thorac Cardiovasc Surg 1975;70:1088–92.

Temporary Double Exclusion of the Perforated Esophagus Using Absorbable Staples

Romeo Bardini, MD, Luigi Bonavina, MD, Maurizio Pavanello, MD,
Massimo Asolati, MD, and Alberto Peracchia, MD

Department of Surgery, University of Padua School of Medicine, Padua, Italy

A new method for double exclusion of the esophagus is presented. Temporary closure of the cervical and intraabdominal esophagus using absorbable staples allows effective healing of esophageal perforations. The procedure should be routinely combined with drainage of the periesophageal abscess. Complete recanalization of the esophagus occurs 1 to 2 weeks after operation.

(Ann Thorac Surg 1992;54:1165–7)

Perforations of the intrathoracic esophagus represent a catastrophic event that necessitates early diagnosis and treatment. The overall mortality rate is about 20% [1, 2] and is related to sepsis from spreading of mediastinal infection through the loose connective tissue surrounding the esophagus.

Ideally, the perforation occurring in a normal esophagus should be treated by early repair through a thoracotomy. However, this is not always possible because of contraindications to thoracotomy or because of a substantial diagnostic delay leading to weakness of the esophageal wall. In such circumstances it is better to proceed with double exclusion of the esophagus. Current surgical techniques include a cervical esophagostomy to drain the salivary flow; this requires a subsequent reconstructive procedure to restore the esophageal transit.

Linear esophageal stapling has been recently proposed as an alternative to conventional procedures to exclude the esophagus [3–6]. This report deals with 2 patients in whom double esophageal exclusion was performed using absorbable staples.

Patients and Methods

From 1975 to April 1992, 130 patients with esophageal perforation were treated in our institution. Ninety-two patients (70.8%) had a perforation of the intrathoracic esophagus. Of these, 61 (66.3%) underwent operation, with a mortality rate of 21.6%. In the last 2 patients of this series, temporary double exclusion of the esophagus using absorbable staples was performed.

The staple (Polysorb 55, US Surgical Corp, Norwalk, CT) is a lactide-glycolic copolymer (Lactomer) fitted to a mechanical stapler (TA 55 Premium Auto Suture, US Surgical Corp). A cartridge with a 4.3-mm distance between the staples is preferable to avoid ischemia of the esophageal wall.

The cervical esophagus is approached through a left cervical incision and is closed with the TA 55. If the perforation is located in the upper mediastinum, this should be drained through the neck. The lower esophagus is approached through a midline laparotomy and is closed with the same stapler. Care is taken to preserve the vagal nerves. If the perforation is located in the lower mediastinum, this should be drained through the abdomen. A feeding jejunostomy is routinely performed. The pleural cavity is drained only if necessary. A soft, double-lumen nasoesophageal tube is left in the proximal esophagus to prevent aspiration of saliva.

Patient 1

A 55-year-old man was admitted to our hospital 20 days after perforation of the midesophagus occurred during endoscopic removal of an impacted meat bolus. About 8 hours later the patient had been treated elsewhere by direct suture of the lesion through a right thoracotomy. A few days later, reoperation consisting of suture and interposition of flap from the latissimus dorsi was performed because of a leak, but it was again unsuccessful. Upon admission to our hospital, the patient was in poor general condition and septic, with a Petzer tube positioned in the right pleural cavity. The esophageal leak was confirmed by a Gastrografin (Schering, Germany) swallow study (Fig 1). Endoscopy showed a lesion of about 5 cm in length on the right posterolateral wall of the esophagus, 27 cm from the incisors.

Double esophageal exclusion was performed using the absorbable staples; the mediastinum and the right pleural cavity were drained, and a feeding jejunostomy was performed. Prompt clinical improvement was noted within a few days. Esophageal recanalization was documented with repeated Gastrografin studies 15 days after the operation (Fig 2). A small residual fistula was completely healed 1 week later, as also shown by endoscopy. The patient started to eat regularly and was discharged.

Patient 2

A 17-year-old girl was sent to our hospital on an emergency basis after perforation of the esophagus occurred during endoscopy; 10 days before she had ingested caustic soda with suicidal purposes. On admission she was febrile, with signs of subcutaneous emphysema of the neck and chest wall; a left chest tube was draining air and

---

Accepted for publication April 7, 1992.

Address reprint requests to Dr Bardini, Via Giustiniani 2, 35128 Padua, Italy.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

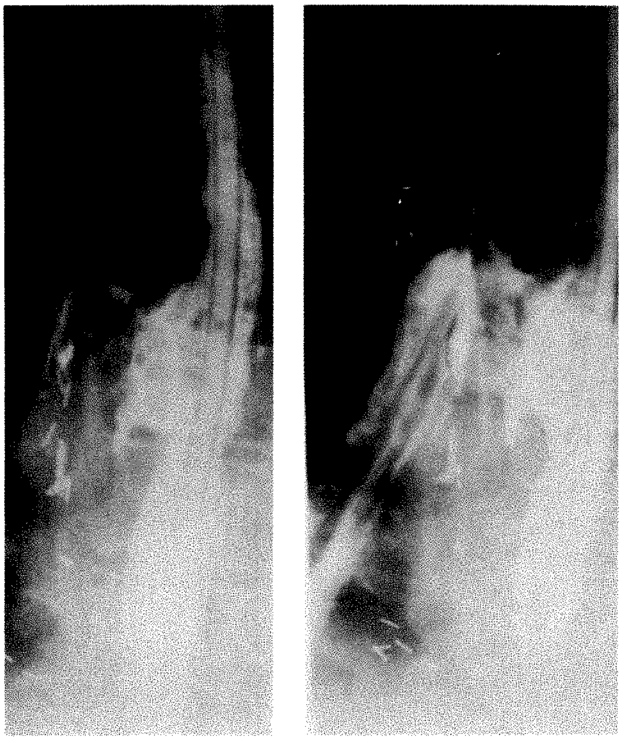


Fig 1. Roentgenogram showing midesophageal perforation.

purulent fluid. The Gastrografin swallow study and the endoscopy showed a lesion of about 1.5 cm in length on the left lateral wall of the esophagus, 35 cm from the incisors (Fig 3).

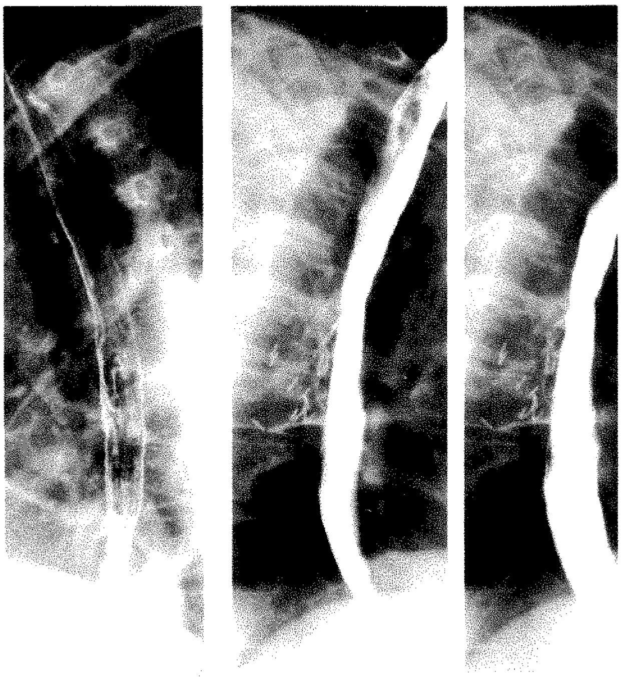


Fig 2. Complete esophageal recanalization 2 weeks after double exclusion with absorbable staples.

Double exclusion of the esophagus with absorbable staples was immediately performed. The mediastinal abscess was drained through the diaphragmatic hiatus. Clinical improvement was dramatic. A Gastrografin swallow study performed 10 days later showed partial recanalization of the esophagus, with only a small fistula drained by the mediastinal tube. Three weeks after the operation the patient started a regular diet, after a roentgenographic study had shown the absence of leaks. A mild esophageal stenosis was related to the previous caustic ingestion (Fig 4). Endoscopy was performed 40 days after operation and showed a mild stenosis (>1 cm) at 36 cm from the incisors. Esophageal dilation was successfully performed using Savary-Gilliard bougies.

Comment

The technique of double exclusion of the esophagus for the treatment of an esophageal perforation was first proposed by Johnson and associates in 1956 [7]. Subsequently, many attempts have been made to simplify the reconstruction of the cervical esophagus after a terminal [8] or lateral [9] cutaneous stoma. Bezard and co-workers [10] suggested opening only the mucosa. Another technique was to insert a Petzer tube or a T tube in the cervical esophagus to drain the saliva, but the results have not always been satisfactory [11]. To exclude the lower esophagus, a gastrostomy has been used most frequently [8, 9]. Esophageal stapling has been advocated [3–5], but persistent closure of the lower esophagus due to the intrinsic properties of the stainless steel staples may require reoperation [6].

Absorbable staples have been used since 1982 in areas in which steel wire was prohibited, such as the vagina and the urinary bladder. Experimental and clinical studies have shown that the Polysorb 55 lactomer copolymer material is absorbed in tissue via hydrolysis and maintains a tensile strength greater than 50% over 2 months [12].

Lower esophageal exclusion with absorbable staples has been advocated for the treatment of the Boerhaave syndrome [6]. However, the possibility of simultaneous closure of the proximal and distal esophagus has raised the question of the timing of recanalization, because some authors believe that an increase in intraesophageal pressure due to delayed opening of the lower esophageal staple line can be detrimental [3]. In our opinion, a double-lumen nasoesophageal tube maintained in the cervical esophagus can avoid this risk by diverting the salivary flow.

We have observed recanalization of the esophagus even 1 week after operation. Although this could not be enough time to obtain complete healing of the esophageal lesion, the application of mediastinal drainages facilitates the healing of a residual fistula, as we noted in the second patient.

We conclude that double esophageal exclusion with absorbable staples is a simple and effective procedure in patients with perforation of the thoracic esophagus. Further experience is needed to verify whether this technique can provide definitive treatment of the perforation in

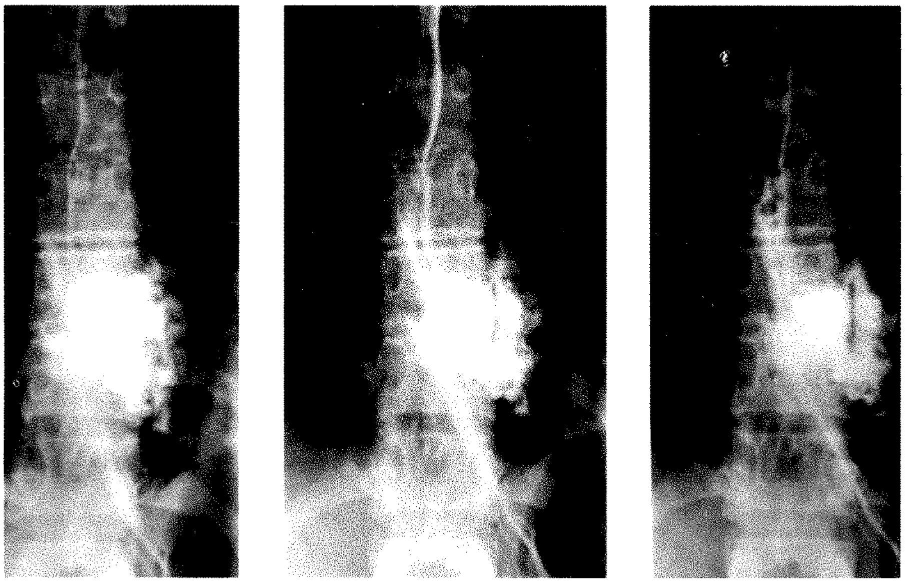


Fig 3. Roentgenogram showing perforation of the lower thoracic esophagus.

selected patients, or whether it should be used in combination with direct suture of the esophageal tear.

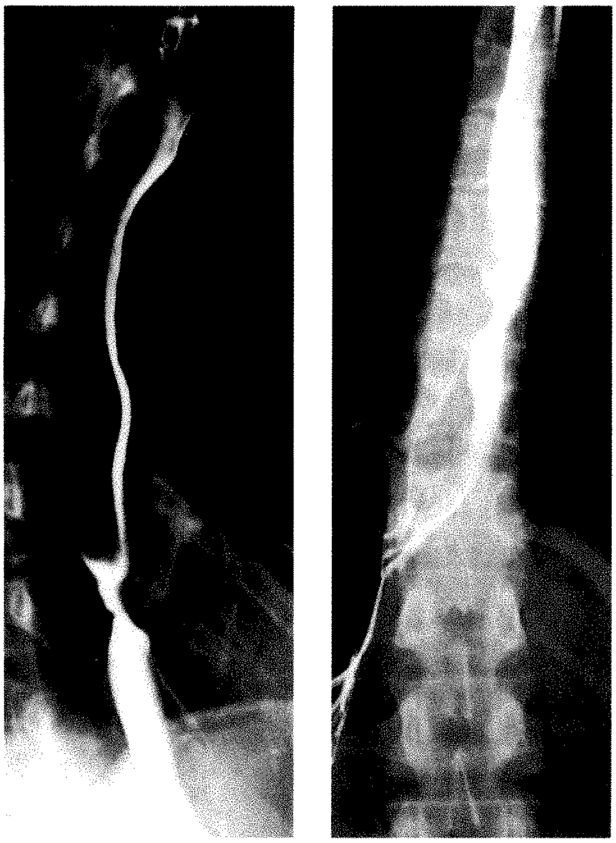


Fig 4. The same patient as in Figure 3 three weeks after operation: the esophageal stenosis is secondary to previous lye ingestion.

References

1. Gayet B, Ancona E. Esophageal perforations II. High risk group patients and treatment. A GEEMO questionnaire. In: Siewert JR, Holscher AH, eds. Diseases of the esophagus. Berlin: Springer Verlag, 1988:1331–6.
2. Jones WG II, Ginsberg RJ. Esophageal perforation: a continuing challenge. Ann Thorac Surg 1992;53:534–43.
3. Assens P, Sarfati E, Guillaume M, Celerier M. L'exclusion temporaire unipolaire ou bipolaire de l'oesophage par agraphage. Presse Med 1984;13:2449–51.
4. Boulez J, Vallette P, Motin J, Clement G, Ducerf C, Chabal J. Problemes posés après exclusion oesophagienne par agraphage. Lyon Chir 1986;82:233–4.
5. Boutelier PH, Lenriot P, Penchet A, Garin B. Exclusion oesophagienne temporaire par agraphage dans les ruptures de l'oesophage thoracique. Chirurgie 1986;112:762–5.
6. Vidrequin A, Mangin P, Beck M, Bresler L, Boissel P, Grosdidier J. Exclusion oesophagienne par agrafes résorbables. Application au traitement conservateur en un temps du syndrome de Boerhaave. Lyon Chir 1988;84:167–8.
7. Johnson J, Schwegman C, Kirby C. Esophageal exclusion for persistent fistula following spontaneous rupture of the esophagus. J Thorac Surg 1956;32:827.
8. Menguy R. Near total esophageal exclusion by cervical esophagostomy and tube gastrostomy in the management of massive esophageal perforation. Ann Surg 1971;173:613–6.
9. Urschel M, Rassuk M, Wood R, Golbraigth W, Pocket P, Paulson D. Improved management of esophageal perforation: exclusion and diversion in continuity. Am Surg 1979; 179:587–91.
10. Bezard J, Lalaude J, Giube J, Vielpeau C, Louis B. Traitement des ruptures spontanées de l'oesophage (Procédé d'oesophagostomie cervicale temporaire). Ann Chir 1973;27:267–70.
11. Lee Y-C, Lee S-T, Chu S-H. New technique of esophageal exclusion for chronic esophageal perforation. Ann Thorac Surg 1991;51:1020–2.
12. Wheeless C. Stapling techniques in operations for malignant disease of the female genital tract. Surg Clin North Am 1984;64:591–608.

Vascular and Interstitial Effect of University of Wisconsin Solution on Canine Lung

Helmut W. Unruh, MD

Respiratory Investigation Unit, Department of Surgery, Faculty of Medicine, The University of Manitoba, Winnipeg, Manitoba, Canada

Belzer's University of Wisconsin cold storage solution (UWCSS) has proved useful in extending the shelf life of organs in extrathoracic transplantation and more recently has also been shown to be useful in heart transplantation. I investigated the effect of 4°C UWCSS on the vascular and interstitial properties of the lung to see whether it affected the pulmonary microcirculation or caused pulmonary edema. Infusion of UWCSS was associated with a slight decrease in oxygen tension, but the final oxygen tension was no different from that previously demonstrated with Euro-Collins solution. Vascular conductance was not affected by UWCSS, but average vascular closure increased slightly, indicating that increased vascular tone occurs. This effect is similar to but less than that previously observed with Euro-Collins solution. Based on comparisons of wet to dry weight ratios, estimates of interstitial compliance, transvascular fluid flux, and microvascular filtration coefficient, it does not appear that UWCSS causes pulmonary edema. Further investigation into the usefulness of UWCSS in lung transplantation is therefore warranted.

(Ann Thorac Surg 1992;54:1168–71)

The most widely used preservation solution for lung transplantation is Euro-Collins solution (ECS). This solution administered at 4°C is known to cause an increase in vascular resistance and is therefore often infused in combination with a potent vasodilator such as prostacyclin [1, 2]. Within the past few years, another solution has become available that allows longer periods of preservation in extrathoracic organ transplantation. The developers of the University of Wisconsin cold storage solution (UWCSS) commented on its potential use and possible problems in lung preservation in an editorial [3] on the principles of solid-organ preservation. This solution is now also being used in clinical situations for heart preservation [4]. Hirt and colleagues [5] recently compared UWCSS with ECS infusions in heterotopic and orthotopic canine lung transplants. They demonstrated improved oxygenation and lower pulmonary vascular resistance in lungs preserved with UWCSS.

My associates and I [1] previously described a canine isolated left lower lobe lung model that was used to systematically study the effect of 4°C ECS and prostacyclin on the pulmonary circulation. In the present study, I undertook to assess whether UWCSS could be used for lung preservation and also to address some of the concerns raised by Belzer and Southard [3]. The effect of UWCSS on gas exchange, pulmonary circulation, and development of edema was examined.

Material and Methods

Nine healthy adult mongrel dogs were anesthetized with sodium pentobarbital (30 mg/kg), intubated, and ventilated with a small animal respirator. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (NIH Publication No. 85-23, revised 1985).

The experimental preparation has previously been described in detail [1]. In brief, after a left thoracotomy and full anticoagulation with heparin sodium, the left lower lobe artery, vein, and bronchus were cannulated. The lobe was excised and suspended from a force transducer for continuous monitoring of weight in the range of 100 mg. The lobe was perfused by gravity with autologous blood warmed to 37°C from inflow to outflow reservoirs of variable height. The bronchial cannula was connected to a 100% oxygen source. From the outflow reservoir, blood was pumped with a roller pump through a heat exchanger, filter, inflow reservoir, and flowmeter. Inflow (Pi), outflow (Po), and airway pressures and flow were all continuously monitored. The preparation is depicted in Figure 1.

The excised lobe was perfused under zone 3 conditions as described by West and associates [6] with airway pressure of 5 cm H_2O, Po of approximately 14 cm H_2O, and initial Pi of 18 to 20 cm H_2O. After stabilization of the preparation, a baseline total wet weight (WW) of the lobe and its tubing was obtained. The Pi and Po were then lowered and matched to approximately 12 cm H_2O, establishing a state of no flow. Once the weight signal indicated no change, Pi and Po were simultaneously raised an equal amount to effect a vascular volume change while maintaining zero flow. Three steps up and three steps down were performed to generate pressure–volume curves from which six calculations of vascular compliance were made (Fig 2). Compliance was calculated by dividing the vascular volume change by the applied pressure.

Accepted for publication April 8, 1992.

Address reprint requests to Dr Unruh, The University of Manitoba Health Sciences Center, 107-671 William Ave, Winnipeg, Man, Canada R3E 0Z2.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

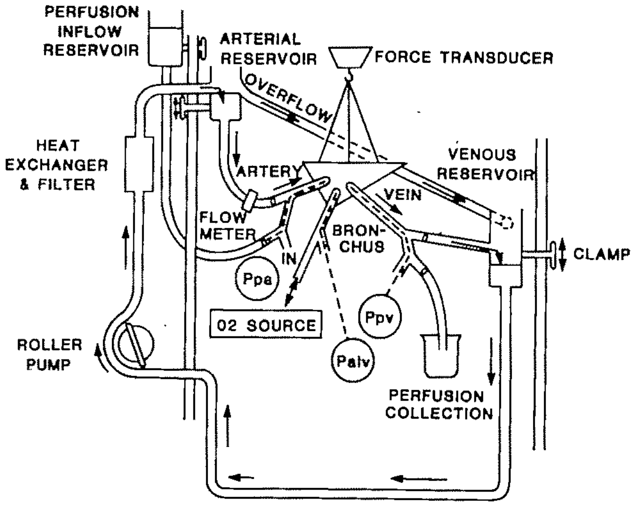


Fig 1. Isolated lobe preparation. Blood flows through the lobe from inflow to outflow reservoirs of variable height. It passes through a heat exchanger and filter before it is returned to the inflow reservoir by a roller pump. A parallel circuit is depicted for the infusion of University of Wisconsin cold storage solution. (Reproduced from Unruh H, Hoppensack M, Oppenheimer L. Vascular properties of canine lungs perfused with Eurocollins solution and prostacyclin. Ann Thorac Surg 1990;49:292–8, by permission.)

Vascular volume changes were arbitrarily considered to be complete 0.6 minute after the onset of a change.

Once the compliance measurements were completed, Pi and Po were raised from 12 cm H_2O to approximately 20 cm H_2O, again maintaining zero flow. After the vascular volume change, there was a slow weight gain, which was attributed to interstitial edema accumulation as the Starling forces balanced themselves. The weight signal was followed for approximately 20 minutes until no change and no further increase were noted, indicating equalization of hydrostatic and osmotic forces.

The weight gain caused by edema was divided by the change in pressure to calculate the interstitial compliance.

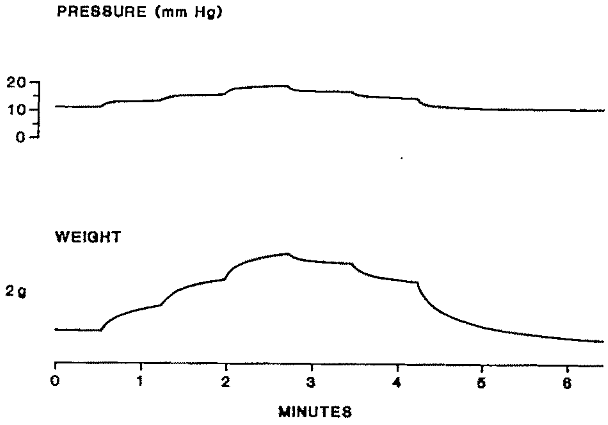


Fig 2. Pressure–volume curves of the lobar circulation. A pressure change was associated with an acute change in weight. The weight change at 0.6 minute after the increase in pressure was taken as the vascular volume change.

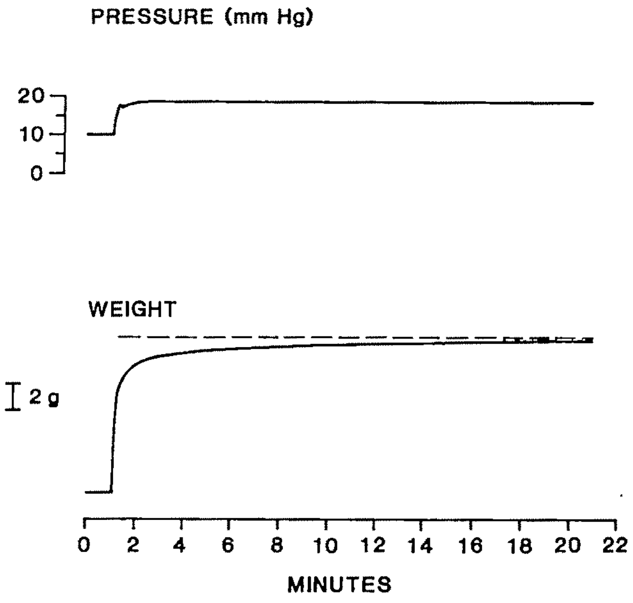


Fig 3. Pressure–volume curve for the interstitial space. After the vascular volume change, the slower rate of weight gain was followed until a new isogravimetric state was achieved. The total weight gained during the slow phase was related to the pressure and time to calculate the interstitial compliance, transvascular fluid flux, and microvascular filtration coefficient.

The edema-related gain was also divided by the time required to become isogravimetric to calculate the interstitial transvascular fluid flux (Q_f) (Fig 3). The slope of the mean microvascular pressure/Q_f curve defines the microvascular filtration coefficient (K_f). Estimates of K_f were calculated by dividing Q_f by the applied pressure and correcting for dry weight (DW) [7–9].

Flow was reestablished, and starting at a Pi of approximately 18 cm H_2O, multiple step increments in Pi were made to generate a pressure–flow profile of the lobar circulation. The outflow reservoir was always adjusted to keep Po at 14 cm H_2O. Vascular conductance, average vascular closure (Cx), and vascular compliance were calculated [1]. Blood gas tensions and hematocrit were

Table 1. Lobar Weights and Vascular Effect of University of Wisconsin Solution[a]

Variable	Baseline (n = 9)	After Infusion (n = 9)
WW/DW ratio	4.4 ± 1.2	5.0 ± 1.3
Infusion time (min)	22.4 ± 4.9	. . .
Rewarming time (min)	. . .	30.8 ± 12.2
Cv (mL · min^{-1} · cm H_2O^{-1})	22.4 ± 10.5	22.0 ± 9.1
Cx (cm H_2O)	11.9 ± 1.6	12.7 ± 1.3[b]
V (mL/cm H_2O)	0.82 ± 0.4	0.75 ± 0.5

[a] Where applicable, data are shown as the mean ± the standard deviation. [b] Significance: $p < 0.05$ versus baseline value.

Cv = vascular conductance; Cx = average vascular closure; V = vascular compliance; WW/DW = wet weight to dry weight.

Table 2. Blood Gas Tensions and Hematocrit[a]

Variable	Baseline	After Infusion
Po_2 (mm Hg)	395 ± 63	338 ± 55
Pco_2 (mm Hg)	14.8 ± 2.5	13.7 ± 2.9
pH	7.64 ± 0.09	7.57 ± 0.08
Hematocrit	0.39 ± 0.06	0.41 ± 0.04

[a] Data are shown as the mean ± the standard deviation.

Pco_2 = carbon dioxide tension; Po_2 = oxygen tension.

measured. These measurements collectively were the baseline determinations.

One liter of 4°C UWCSS, fully excluded from the circuit, was infused at an inflow pressure of no more than 15 cm H_2O over about 30 minutes. Oxygen flow was continued during the infusion, as my colleagues and I [1] previously demonstrated that this has a beneficial effect during ECS infusion. After rewarming, the studies were repeated. Then the lobe was weighed to obtain its final wet weight (WW), drained of blood, and dried completely by blowing dry air through the bronchus for 24 hours followed by baking to a constant DW.

Each dog served as its own control. Therefore, for comparisons within groups, paired *t* tests were used. Analysis of variance was used to compare the pressure–volume curves of the lobar circulation.

Results

The effect of UWCSS on the WW to DW ratios, infusion times, rewarming times, and vascular properties are summarized in Table 1. The solution did not increase the WW/DW ratio. Vascular conductance and vascular compliance were not changed with UWCSS infusion, but there was a slight and significant increase in Cx (mean difference, 0.82 ± 0.34 [standard error]; $p < 0.05$).

The effect of UWCSS on gas exchange is summarized in Table 2. The oxygen tension after infusion was marginally but significantly different ($p < 0.05$) from the baseline value. The hematocrit, carbon dioxide tension, and pH were unchanged.

The effect of UWCSS on the interstitial properties of the lung are given individually for all dogs in Table 3. There was no difference in interstitial compliance and Q_f, but K_f estimates significantly decreased (mean difference, $7.3 \times 10^{-5} \pm 8.8 \times 10^{-5}$ [standard deviation]; $p < 0.05$) after infusion of UWCSS.

Comment

The potential use of UWCSS in thoracic organ transplantation has not been fully established. It has proved to be very useful in kidney, liver, and pancreatic transplantation.

The vascular effects of UWCSS were assessed in the same manner my colleagues and I [1] used for ECS. Euro-Collins solution with and without prostacyclin resulted in a significant decrease in vascular conductance, whereas no change in this variable was observed with UWCSS in the present study. In the previous study [1], Cx increased with ECS, and this was overcome by the addition of prostacyclin. The UWCSS caused an increase in Cx of a similar degree to that previously seen with ECS alone. This indicates, according to our previous method of analysis [1], that UWCSS infused at 4°C causes increased vascular tone but not the vascular obstruction that accompanies it with ECS infusion. The increased tone may also respond to prostacyclin, as was the case with ECS, but the necessity for this is not immediately apparent. The increase in Cx was only 60% of that seen with ECS, and this, combined with the fact that vascular conductance was unaltered, raises uncertainty about its actual importance.

In this study, the focus was primarily on the acute microvascular effects of UWCSS. The effects of UWCSS have been studied by others after longer periods of

Table 3. Interstitial Properties

	I_c (g/cm H_2O)		Q_f (g/min)		P (cm H_2O)		K_f (mL · min^{-1} · cm H_2O^{-1} · g^{-1} DW)	
Dog No.	I	II	I	II	I	II	I	II
1	0.93	0.34	0.25	0.27	22.75	28	0.00063	0.00055
2	1.0	0.44	0.23	0.22	19.5	18.25	0.0012	0.0012
3	0.41	1.77	0.22	0.11	23.5	16.5	0.00089	0.00064
4	0.71	1.05	0.21	0.20	23.5	25	0.00065	0.00059
5	0.20	0.12	0.081	0.052	20.25	20.5	0.00029	0.00018
6	0.62	0.48	0.29	0.28	19	19	0.0011	0.0011
7	0.56	0.30	0.20	0.20	19.75	20	0.00086	0.00086
8	1.0	0.61	0.27	0.20	16.75	16	0.00087	0.00071
9	0.34	0.37	0.24	0.24	19	18.75	0.0011	0.0011
Mean ± SD	0.64 ± 0.3	0.61 ± 0.5	0.22 ± 0.6	0.20 ± 0.2	. . .	. . .	0.00084 ± 0.00029	0.00077 ± 0.00033[a]

[a] Significance: *p* 0.05 versus value at I.

DW = dry weight; I_c = interstitial compliance; K_f = microvascular filtration coefficient; P = pressure at which K_f estimated; Q_f = transvascular fluid flux; SD = standard deviation; I = baseline values; II = values after rewarming.

ischemia. Naka and co-workers [10] reported a 53% increase in pulmonary vascular resistance after 24 hours of ischemia in canine heterotopic heart-lung transplants. However, Kawahara and associates [11] found that a similar ischemic interval in an excised intact left lung preparation was not associated with an increase in pulmonary vascular resistance. Miyoshi and colleagues [12] found that mean pulmonary artery pressure in a rabbit lung preparation was elevated after 30 hours of ischemia when preserved in UWCSS compared with preservation in a low-potassium dextran solution. Substantial evidence is therefore beginning to accumulate to the effect that UWCSS does affect pulmonary vascular resistance, albeit not to the same extent as ECS [1, 11]. This effect, demonstrated in the present study as an increase in Cx or vascular tone, may become amplified as the ischemic time lengthens. To date, there is not substantial evidence concerning the effects of UWCSS after variable periods of ischemia in the lung other than that recently reported by Aeba and colleagues [13]. They compared 6 to 12 hours of ischemia and noted significant deterioration in gas exchange and lipid peroxide concentration and a tendency toward increased WW/DW ratios over time.

Concern has been raised that UWCSS might cause pulmonary edema [3]. Infusion of 1 L did not increase the WW/DW ratio significantly or change interstitial compliance and Q_f. The WW/DW ratio did increase by 14%, which may have physiologic importance. However, with the relatively large standard deviation, this difference did not achieve statistical significance. There was a small but significant decrease in estimated K_f. Transvascular fluid flux is directly proportional to K_f, and therefore a decrease reflects a less permeable or more stable membrane after UWCSS infusion. The K_f was estimated from a single determination of Q_f, and there are, therefore, limitations to the interpretation that can be drawn from the data. The individual values are in the range of those published for excised lungs [14]. The decrease in K_f is therefore consistent with the other observations of no change in WW/DW ratio, interstitial compliance, and Q_f.

In general, studies that have employed longer periods of ischemia have reported a significant increase in WW/DW ratios compared with control or baseline conditions [10, 11, 13]. The observations in the present study have some support in the findings of Aeba and associates [13]. Their WW/DW ratios after flush and ischemia alone were lower than those at control conditions. Reperfusion, however, was associated with a marked increase in WW/DW ratios. Therefore, the ischemic period may have exceeded the capacity of UWCSS to protect the lung.

University of Wisconsin cold storage solution increases vascular resistance in the lung but to a lesser extent than ECS alone. Infusion of UWCSS is not associated with and does not appear to cause pulmonary edema acutely. Over more prolonged periods of ischemia, the use of UWCSS in the lung may be associated with progressive edema accumulation, but, in general, other variables of functional integrity such as gas exchange tend to be maintained. Further investigation into the applicability of UWCSS in lung transplantation is therefore warranted.

Supported by a grant from the Heart and Stroke Foundations of Canada.

University of Wisconsin cold storage solution donated by Dupont Canada.

References

1. Unruh H, Hoppensack M, Oppenheimer L. Vascular properties of canine lungs perfused with Eurocollins solution and prostacyclin. Ann Thorac Surg 1990;49:292–8.
2. Novick RJ, Reid KR, Denning L, Duplan J, Menkis AH, McKenzie FN. Prolonged preservation of canine lung allografts: the role of prostaglandins. Ann Thorac Surg 1991;51:853–9.
3. Belzer FO, Southard JH. Principles of solid-organ preservation by cold storage. Transplantation 1988;45:673–6.
4. Stein DG, Drinkwater DC, Laks H, et al. Cardiac preservation in patients undergoing transplantation. A clinical trial comparing University of Wisconsin solution and Stanford solution. J Thorac Cardiovasc Surg 1991;102:657–65.
5. Hirt SW, Wahlers T, Jurmann MJ, et al. University of Wisconsin versus modified Euro-Collins solution for lung preservation. Ann Thorac Surg 1992;53:74–9.
6. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung: relation to vascular and alveolar pressures. J Appl Physiol 1964;19:713–24.
7. Drake RE, Gaar KA, Tayler AE. Estimation of the filtration coefficient of pulmonary exchange vessels. Am J Physiol 1978;243(Heart Circ Physiol):H266–74.
8. Drake RE, Smith JH, Gabel JC. Estimation of the filtration coefficient in intact dog lungs. Am J Physiol 1980;238(Heart Circ Physiol):H430–8.
9. Drake RE, Gabel JC. Comparison of techniques to measure pulmonary filtration coefficients in dogs. Microvasc Res 1981;21:133–44.
10. Naka Y, Shirakura R, Matsuda H, et al. Canine heart-lung transplantation after twenty-four-hour hypothermic preservation with Belzer-UW solution. J Heart Lung Transplant 1991;10:296–303.
11. Kawahara K, Ikari H, Hisano H, et al. Twenty-four-hour canine lung preservation using UW solution. Transplantation 1991;51:584–7.
12. Miyoshi S, Shimokawa S, Schreinemakers H, et al. Comparison of the University of Wisconsin preservation solution and other crystalloid perfusates in a 30-hour rabbit lung preservation model. J Thorac Cardiovasc Surg 1992;103:27–32.
13. Aeba R, Keenan RJ, Hardesty RL, Yousem SA, Hamamoto I, Griffith BP. University of Wisconsin solution for pulmonary preservation in a rat transplant model. Ann Thorac Surg 1992;53:240–6.
14. Hancock BJ, Hoppensack M, Oppenheimer L. Do transvascular forces in isolated lobe preparations equilibrate? J Appl Physiol 1989;67:628–35.

Low-Dose Aprotinin in Internal Mammary Artery Bypass Operations Contributes to Important Blood Saving

Jacques P. A. M. Schönberger, MD, Peter A. M. Everts, EKP, Husam Ercan, MD, Johan J. Bredée, MD, PhD, Johan H. Bavinck, MD, Eric Berreklouw, MD, and Charles R. M. Wildevuur, MD, PhD

Department of Cardiopulmonary Surgery, Catharina Hospital, Eindhoven, and Department of Cardiopulmonary Surgery, Research Division, University Hospital, Groningen, the Netherlands

The effect on postoperative blood loss and blood use of blood-saving treatment with or without 280 mg of low-dose aprotinin (2 million kallikrein inactivator units) was studied in 200 consecutive patients undergoing either unilateral or bilateral internal mammary artery bypass grafting. Postoperative blood loss and total units of homologous blood products were similar in patients having either bypass procedure without aprotinin treatment. In patients given aprotinin, postoperative blood loss and use of homologous blood products were significantly lower ($p < 0.05$). The use of any donor blood product was prevented in 78% of the patients given aprotinin versus only 45% of patients treated without aprotinin. None of the aprotinin-treated patients underwent repeat thoracotomy for excessive bleeding; repeat thoracotomy was indicated in 8% of the patients having bilateral internal mammary artery grafting without aprotinin treatment. These results demonstrate that low-dose aprotinin reduces blood loss and blood use significantly and prevents excessive bleeding.

(Ann Thorac Surg 1992;54:1172–6)

The internal mammary artery (IMA) is generally accepted as the superior bypass conduit in coronary artery revascularization. Because of the results with the use of one IMA, there is a growing belief that coronary artery bypass grafting should be performed with both IMAs [1]. However, more perioperative complications are observed in bilateral IMA (BIMA) procedures than in single-IMA operations [2]. The most important complication is the increased bleeding tendency after BIMA grafting [3]. This complication increases the risk of donation of blood products and thus the risk of bloodborne infections [4]. Therefore, blood-saving measures in IMA grafting, and specifically BIMA grafting, should be applied.

Because blood loss and blood use can be effectively decreased with a proteinase inhibitor [5], we treated patients undergoing IMA or BIMA grafting with 280 mg of aprotinin added to the pump prime (2 million kallikrein inactivator units [KIU]) as well as our current blood-saving program. We analyzed the postoperative blood loss and the need for or prevention of the use of any homologous blood products in unilateral IMA and BIMA procedures with and without aprotinin treatment. The incidence of repeat thoracotomy for excessive bleeding with and without low-dose aprotinin treatment was also studied.

Material and Methods

Retrospectively we compared 100 patients who were treated with aprotinin and underwent primary isolated coronary artery bypass grafting with one or both IMAs with 100 patients who underwent similar operative procedures but received no aprotinin. In addition, saphenous vein bypass grafting was performed when appropriate. All patients were operated on between May 1989 and August 1990.

The patients were allocated to one of four groups:

Group 1 (n = 50): IMA grafting without intraoperative treatment with aprotinin
Group 2 (n = 50): BIMA grafting without intraoperative treatment with aprotinin
Group 3 (n = 50): IMA grafting with aprotinin treatment (200 mL of an aprotinin solution [Bayer, AG, Leverkusen, Germany] containing 280 mg of aprotinin [2 million KIU] added to the pump prime of the extracorporeal circuit)
Group 4 (n = 50): BIMA grafting with aprotinin as in group 3.

To match closely the four patient groups, patients included in the study had a similar sex distribution by group, had a hemoglobin level before bypass of 142 ± 10 g/L (14.2 ± 1.0 g/dL), and underwent identical operative procedures by group. In all patients, administration of anticoagulants and platelet inhibitors was discontinued at least 5 days before operation.

Accepted for publication April 9, 1992.

Address reprint requests to Dr Schönberger, Catharina Hospital, Michelangelolaan 2, 5602 ZA, PO Box 1350, Eindhoven, the Netherlands.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Anesthesia Management

Induction of anesthesia consisted of preoxygenation, 20 mg of etomidate, 1 mg of fentanyl, and 8 mg of pancuronium bromide. Maintenance of anesthesia before bypass consisted of 50% oxygen in air, 1 to 3 mg of fentanyl, and 8 mg of pancuronium. Nitrates were given intravenously to control systemic and pulmonary artery pressures.

Surgical Management

After the opening of the pleural space or spaces, the left IMA for unilateral bypass grafting and then the right IMA for bilateral bypass grafting were harvested with cautery from the subclavian vein down to the sixth intercostal space. Side branches were clipped with small clips. In all instances, the pericardium was incised under or above the phrenic nerve. Through this pericardial slit, the course of the arterial conduit or conduits was smooth from the subclavian artery to the coronary artery anastomoses. The pericardial slit was not closed, and the pleura or pleurae were left wide open.

Bovine lung heparin (250 IU/kg) was given intravenously 5 minutes before cannulation. An additional bolus of heparin (5,000 IU) was administered every half hour.

The extracorporeal circuit consisted of a hollow-fiber oxygenator (Sarns, Ann Arbor, MI), a cardiotomy reservoir (model D742; Dideco SpA, Mirandola, Italy), and an arterial line filter (Swank; Cobe Laboratories, Inc, Lakewood, CO). The circuit was primed with 1,500 mL of urea-linked gelatin (Haemaccel; Hoechst, Behringwerke AG, Marburg, Germany) containing 5,000 IU of bovine lung heparin and 100 mL of mannitol. The perfusion flow rate at moderate hypothermia of 28° to 32°C was 2.5 $L \cdot min^{-1} \cdot m^{-2}$.

After aortic cross-clamping, cardioplegia was induced with 1,000 mL of cold (4°C) St. Thomas' Hospital solution and maintained with 500 mL every half hour. When blood cardioplegia was preferred by the surgeon, cardioplegia was achieved with an induction dose of 1,000 mL. Blood cardioplegic solution was administered every 20 minutes at a dose of 500 mL through the aortic root or venous grafts or retrogradely through the coronary sinus, whichever was most convenient. Warm blood cardioplegic solution (500 mL) was administered before the declamping of the aorta.

For external cardiac cooling, cold (4°C) saline solution was used. The mixture of blood and external cooling fluid, collected in the pericardium and pleural space, was returned to the extracorporeal circuit. At the end of perfusion, protamine sulfate was infused to neutralize the total dose of heparin.

Blood-Saving Program

Regardless of the operative procedure or administration of aprotinin, all patients were treated during and after the operation according to a blood-saving program. Autologous blood was withdrawn before bypass through the venous cannula after heparinization when the absence of ischemia or hemodynamic instability allowed removal. At the end of the operation after protamine administration, the autologous blood was retransfused. After aortic decannulation, residual volume in the extracorporeal circuit was collected in blood transfusion bags and retransfused gradually. Packed cells were administered when the postoperative hematocrit fell to less than 0.25. In patients older than 70 years, a hematocrit of less than 0.30 was not accepted.

Blood Requirements and Blood Loss

Homologous blood requirements during and after the operation were registered. The postoperative blood loss was measured in each patient. The shed mediastinal blood was collected for 18 to 24 hours after the operation in a Pleur-evac system (Deknatel GMBH, Neustadt, Germany) in which a negative intrapleural pressure of 25 cm H_2O was applied.

Repeat thoracotomy for bleeding was indicated when more than 800 mL of shed blood was lost within the first 2 hours after arrival of the patient in the intensive care unit or when 1,000 mL was lost within 3 hours after operation.

The bleeding time was determined in all patients by a modified simplate II method on the day before operation. The platelet count and the hemoglobin level during hospitalization were recorded for each patient.

Statistical Analysis

All values were expressed as the mean ± the standard error of the mean. Statistical analysis was achieved by unpaired t testing. A p value of less than 0.05 was considered significant.

Results

Patient characteristics were similar before and during the operation in the four groups except for the mean age, which was less in patients having BIMA grafting than in patients having single IMA grafting (Table 1).

Blood Loss and Blood Requirements in Groups 1 and 2

Patients undergoing IMA or BIMA procedures without aprotinin treatment had a similar blood loss postoperatively. Repeat thoracotomy for bleeding was performed in 4 patients (8%) undergoing BIMA grafting (Table 2). In all 4 patients, oozing was the cause of blood loss.

The total requirements of homologous blood products were similar in both groups (Table 3). In 42% of the patients having IMA grafting and in 48% of those undergoing BIMA grafting, the need for any blood product could be prevented with our standard blood-saving techniques (Fig 1). Table 4 shows the results of these techniques.

Blood Loss and Blood Requirements in Groups 3 and 4

Compared with groups 1 and 2, the aprotinin-treated patients had a significantly decreased ($p < 0.05$) postoperative blood loss. However, the loss was significantly more reduced ($p < 0.01$) in patients undergoing unilateral IMA grafting compared with those having bilateral procedures. No repeat thoracotomies for excessive bleeding

Table 1. Summary of Patient Data[a]

	Group			
Variable	1: IMA− (n = 50)	2: BIMA− (n = 50)	3: IMA+ (n = 50)	4: BIMA+ (n = 50)
Sex				
Male	43	43	43	43
Female	7	7	7	7
Age (y)[b]	58 ± 0.8	51 ± 1.0	58 ± 1.1	54 ± 1.1
BSA (m^2)	1.89 ± 0.3	1.89 ± 0.2	1.88 ± 0.3	1.90 ± 0.2
No. of grafts	3.2 ± 0.2	3.3 ± 0.17	3.2 ± 0.17	3.1 ± 0.2
Hb before bypass (g/dL)	14.2 ± 0.2	14.1 ± 0.2	14.1 ± 0.2	14.2 ± 0.2
Perfusion time (min)	91 ± 5.6	86 ± 4.8	82 ± 4.1	88 ± 4.1
Cross-clamp time (min)	53 ± 5.1	48 ± 3.2	47 ± 3.5	51 ± 3.2
Myocardial infarction (%)	0	2	2	0

[a] Where applicable, data are shown as the mean ± the standard error of the mean. [b] Patients in groups 1 and 3 were significantly older ($p < 0.01$) than patients in groups 2 and 4.

BIMA = bilateral internal mammary artery bypass grafting; BSA = body surface area; Hb = hemoglobin level; IMA = unilateral internal mammary artery bypass grafting; + = with aprotinin treatment; − = without aprotinin treatment.

were required in the patients receiving aprotinin (see Table 2).

The need for any blood products was drastically decreased in patients treated with aprotinin (see Table 3). When aprotinin was added to our standard blood-saving techniques, the administration of blood products was prevented in 78% of the patients undergoing either IMA or BIMA operations (see Fig 1).

The mean template bleeding time on the day before operation was similar in all four groups. The platelet counts and the hemoglobin levels during hospitalization were identical in all four groups. No sequelae of aprotinin treatment (eg, allergic reactions or an increased myocardial infarction rate) were observed (see Table 1).

Comment

By adding low-dose aprotinin to the pump prime, we prevented the need for repeat thoracotomy, reduced blood loss substantially, decreased the total use of blood products by approximately 75%, and most importantly, avoided the use of any homologous blood product in 78% of patients.

One of the major disadvantages of BIMA bypass grafting, a higher risk of repeat thoracotomy, was eliminated with low-dose aprotinin. Lytle and associates [2] in 1986 and Henze and co-workers [3] in 1989 reported an incidence of repeat thoracotomy of 11.8% and 9%, respectively, in patients having BIMA grafting. In agreement with their findings, 8% or 4 of our patients underwent reoperation for bleeding after BIMA procedures. Henze and associates [3] and Cosgrove and colleagues [6] demonstrated that excessive bleeding is an important risk almost exclusively after BIMA grafting, as repeat thoracotomy for excessive bleeding in patients after single IMA grafting was indicated in only 1.9% and 2.1%, respectively, of their patients (none in our study).

With the reduction in blood loss effected by aprotinin, we came close to the standard of blood saving set by Cosgrove and co-workers [6] for IMA operations: a mean of 0.5 unit in our patients versus 0.2 unit of homologous blood in their patients. Twenty-two percent of our patients and 16% of their patients needed blood products during and after IMA grafting. Lytle and colleagues [2] reported that the need for bank blood was 1.3 units in BIMA grafting, whereas we reached 0.6 unit in our patients having bypass grafting with both IMAs when aprotinin was added to the pump prime. The use of any blood product was prevented in 67.5% of their patients

Table 2. Postoperative Blood Loss and Repeat Thoracotomy[a]

	Group				Differences Between Groups	
Variable	1: IMA−	2: BIMA−	3: IMA+	4: BIMA+	Comparison	*p* Value
Postop blood loss (mL)	1,237 ± 93	1,404 ± 135	684 ± 57	1,055 ± 80	1 vs 2	NS
					3 vs 4	<0.01
					1 vs 3	<0.01
					2 vs 4	<0.05
Repeat thoracotomy (%)	0	8	0	0	. . .	. . .

[a] Blood loss data are shown as the mean ± the standard error of the mean.

NS = not significant; other abbreviations are the same as in Table 1.

Table 3. Use of Blood Products[a]

	Group				Differences Between Groups	
Variable	1: IMA−	2: BIMA−	3: IMA+	4: BIMA+	Comparison	*p* Value
Packed cells (U)	1.2 ± 0.2	1.3 ± 0.3	0.4 ± 0.1	0.4 ± 0.1	1 vs 2	NS
					3 vs 4	NS
					1 vs 3	<0.01
					2 vs 4	<0.01
Fresh frozen plasma (U)	0.4 ± 0.1	1.1 ± 0.3	0.2 ± 0.1	0.2 ± 0.1	1 vs 2	<0.05
					3 vs 4	NS
					1 vs 3	NS
					2 vs 4	<0.01
Total units	1.6 ± 0.3	2.5 ± 0.7	0.5 ± 0.2	0.6 ± 0.2	1 vs 2	NS
					3 vs 4	NS
					1 vs 3	<0.01
					2 vs 4	<0.01

[a] Data are shown as the mean ± the standard error of the mean.

NS = not significant; other abbreviations are the same as in Table 1.

having BIMA grafting versus 78% of our patients receiving aprotinin.

This finding contrasts with the result obtained with our standard blood-saving program, ie, without the use of aprotinin, consisting of withdrawal of autologous blood before bypass, infusion of the residual volume in the extracorporeal circuit after decannulation, and the acceptance of normovolemic anemia postoperatively. With this standard blood-saving program, we avoided the use of any blood products in approximately 45% of the patients undergoing IMA or BIMA bypass grafting. In our patients treated with aprotinin, the postoperative blood loss and blood requirements were reduced in single IMA procedures by 25% and 75%, respectively, and in BIMA procedures by 45% and 70%, respectively. Therefore, aprotinin, the only different factor between the aprotinin-treated and untreated groups, plays a crucial role in addition to our standard blood-saving program.

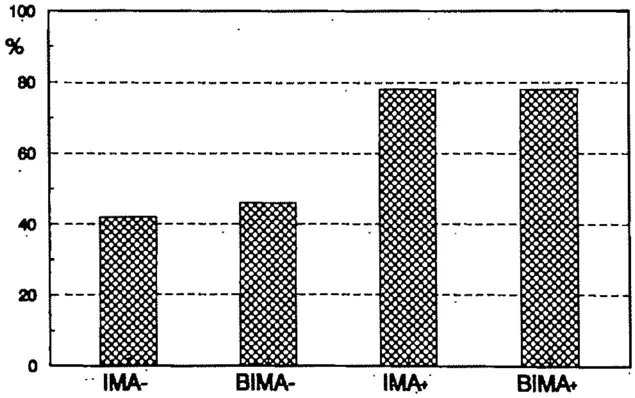


Fig 1. Percentage of patients receiving no blood products. Patients in groups 1 and 2 received significantly more (p < 0.01) homologous blood products than patients in groups 3 and 4. (BIMA = bilateral internal mammary artery bypass grafting; IMA = unilateral internal mammary artery bypass grafting; + = with aprotinin treatment; − = without aprotinin treatment.)

The discrepancy between a rather small reduction in blood loss and a much more pronounced reduction in the need for blood products, as observed in our patients, was also noticed by Bidstrup and associates [7]. They showed that the hemoglobin level in the shed blood, rather than the volume of the shed blood, was diminished in patients undergoing coronary artery bypass grafting with aprotinin treatment. This finding explains the dramatic decrease in blood requirements associated with a lower, but still substantial reduction in the volume of shed blood in their patients.

The clinical beneficial effects of aprotinin in high dose (6 million KIU) on blood loss and blood use in coronary artery bypass procedures are well demonstrated in several prospective, randomized studies [7, 8]. However, studies on the blood-saving effect of low-dose aprotinin produced contrary data. Scott and Au [9] noted no significant effect on blood loss and blood requirements in patients treated with low-dose aprotinin (2.5 million KIU) administered intraoperatively before, during, and after bypass. Covino and associates [10], however, noticed an important blood-saving effect in their patients with a similar dosage regimen of aprotinin. Their result was in agreement with the observation of van Oeveren and colleagues [5], who found that a single dose of 2 million KIU of aprotinin added to the pump prime contributed to blood salvage. In the same study, this group analyzed the effect on blood saving of a single dose of 2 million KIU versus a multidose regimen of 6 million KIU of aprotinin. Both doses resulted in a similarly important blood saving. For this reason, we chose to use the more practical and less expensive dose of 2 million KIU.

To explain the different results with low-dose aprotinin obtained by van Oeveren and co-workers [5], Scott and Au [9], and Covino and colleagues [10], total bypass time

Table 4. Results of Intraoperative Blood-Saving Techniques[a,b]

Variable	Group 1: IMA−	2: BIMA−	3: IMA+	4: BIMA+
Predonation (mL)	298 ± 74	300 ± 43	341 ± 56	362 ± 67
Residual volume in circuit (mL)	376 ± 45	358 ± 58	372 ± 32	449 ± 48

[a] Data are shown as the mean ± the standard error of the mean. [b] There were no significant differences between groups.

Abbreviations are the same as in Table 1.

might have played an important role. In this regard, van Oeveren and co-workers [5] noticed less favorable effects of low-dose aprotinin when bypass time exceeded 90 minutes. In this situation, the plasma kallikrein-inhibiting capacity of aprotinin decreased below an effective level. Scott and Au [10] reported a bypass time of about 120 minutes with a possibly ineffective plasma level of aprotinin after 90 minutes, whereas Covino and co-workers [10] and our group required less than 90 minutes.

The mechanism of aprotinin on hemostasis is not quite clear but appears to be directly associated with platelet adhesion. Van Oeveren and co-workers [5, 8] showed that the adhesive platelet receptor (GPIb) was similarly preserved against the first-pass effect of extracorporeal circulation either by low-dose or by continuously administered high-dose aprotinin. They noticed no effect of aprotinin on the aggregatory platelet receptors (GPIIbIIIa) during extracorporeal circulation. In agreement with Zilla and colleagues [11], they stressed that impairment of the aggregatory platelet receptor is of minor importance for hemostasis. Nevertheless, they suggested use of a membrane oxygenator instead of a bubble oxygenator, as it provides better preservation of the aggregatory receptors during extracorporeal circulation [12].

We found a similar need of blood products and a similarly large blood loss after both single IMA and BIMA grafting procedures with a substantial risk for excessive bleeding after BIMA operations. Postoperative bleeding and the need for blood products were significantly reduced by adding aprotinin to the pump prime. Complications from the use of aprotinin were not observed. We conclude that adding a single low dose of aprotinin to the pump prime in bypass operations involving one or both IMAs contributes to blood saving.

References

1. Galbut DL, Traad EA, Dorman MJ, et al. Twelve-year experience with bilateral internal mammary artery grafts. Ann Thorac Surg 1985;40:264–70.
2. Lytle BW, Cosgrove DM, Loop FD, Borsh J, Goormastic M, Taylor PC. Perioperative risk of bilateral internal mammary artery grafting: analysis of 500 cases from 1971 to 1984. Circulation 1986;74(Suppl 3):37–41.
3. Henze A, Ramstrom J, Nystrom SO. Bilateral internal mammary artery for coronary revascularization. Scand J Thorac Cardiovasc Surg 1989;23:9–12.
4. Peterman TA. Transfusion associated acquired immunodeficiency syndrome. World J Surg 1987;11:36–40.
5. Van Oeveren W, Harder MP, Roozendaal KJ, Eijsman L, Wildevuur CRH. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:788–97.
6. Cosgrove DM, Loop FD, Lytle BW, et al. Does mammary artery grafting increase surgical risk? Circulation 1985; 72(Suppl 2):170–4.
7. Bidstrup BP, Royston D, Taylor KM, Cosgrove DM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989;97:364–72.
8. Van Oeveren W, Jansen NJG, Bidstrup BP, et al. Effects of aprotinin on hemostatic mechanisms during cardiopulmonary bypass. Ann Thorac Surg 1987;44:640–5.
9. Scott DHT, Au J. The Edinburgh experience—low-dose Trasylol. In: Friedel N, Hetzer R, Royston D, eds. Blood use in cardiac surgery. Darmstadt: Steinkopff Verlag; New York: Springer-Verlag, 1991:263–5.
10. Covino E, Iorio D, Marino L, Ferrara P, Spampinato N. Low dose aprotinin as blood saver in open heart surgery. Eur J Cardiothorac Surg 1991;5:414–8.
11. Zilla P, Fasol R, Groscurth P, Klepetko W, Reichenspurner H, Wolner E. Blood platelets in cardiopulmonary bypass operations. Recovery occurs after initial stimulation, rather than continual activation. J Thorac Cardiovasc Surg 1989;97: 379–88.
12. Edmunds LH, Ellison N, Colman RW, et al. Platelet function during cardiac operation. Comparison of membrane and bubble oxygenators. J Thorac Cardiovasc Surg 1982;83: 805–12.

Safety and Efficacy of Autologous Blood Donation Before Elective Aortic Valve Operation

Walter H. Dzik, MD, Arlen G. Fleisher, MD, David Ciavarella, MD, Karl J. Karlson, MD, George E. Reed, MD, and Robert L. Berger, MD

Departments of Pathology and Surgery, New England Deaconess Hospital, and Departments of Medicine and Surgery, Harvard Medical School, Boston, Massachusetts; and Departments of Medicine, Pathology and Surgery, Westchester County Medical Center and New York Medical College, Valhalla, New York

Although the use of preoperative autologous blood donations for patients undergoing elective cardiac operations has increased dramatically in recent years, patients awaiting elective aortic valve replacement have traditionally been denied access to preoperative autologous blood collection programs. We report our experience with 79 patients, each of whom donated 1 to 3 units of autologous blood before an aortic valve operation. All patients had serious aortic valve disease as evidenced by symptoms and preoperative catheterization data. The patients collectively made 129 blood donations. One patient had a syncopal episode within 2 hours of donation and recovered without difficulty. Of the patients who gave autologous blood preoperatively, 68% avoided any homologous blood donor exposure during their subsequent hospitalization for aortic valve replacement. In contrast, in a group of 298 patients who did not give autologous blood preoperatively, only 31% avoided homologous blood exposure during aortic valve replacement ($p <$ 0.0001). Our experience suggests that preoperative autologous blood donation by patients awaiting elective aortic valve replacement is both safe and effective. Patients with aortic valve disease should not be routinely excluded from preoperative blood services.

(Ann Thorac Surg 1992;54:1177–81)

The last few years have witnessed an unprecedented growth in the use of autologous blood donated before elective operations [1]. Despite the advantages of autologous blood, patients with aortic stenosis or aortic insufficiency awaiting aortic valve replacement have been denied access to preoperative autologous blood donations because of concern about the potential for serious complications from the procedure [2, 3]. For patients with aortic stenosis concern has existed that the acute volume depletion (475 mL) of blood donation might compromise cardiac output or that the vasodilatation resulting from a vasovagal donor reaction might precipitate shock. Moreover, for some patients the lower red cell mass induced by preoperative blood donations may be inadequate to meet the increased myocardial oxygen demand of the hypertrophied heart. Although the literature suggests that patients with aortic stenosis should be excluded from donation, in practice most blood donor programs exclude all patients awaiting aortic valve replacement because many patients have mixed aortic stenosis/aortic insufficiency lesions and because reliable information on the degree of aortic stenosis is usually not available to the blood collection facility. We were unable to find documentation in the literature of increased complications resulting from autologous blood donations by patients awaiting aortic valve replacement. We therefore chose to offer this service to patients with aortic valve disease awaiting valve replacement and report the results from our experience with 79 consecutive patients.

Material and Methods

Patients with symptomatic aortic valve disease scheduled for elective valve replacement at the Westchester County Medical Center, Valhalla, NY, and at the New England Deaconess Hospital, Boston, MA, were referred for preoperative autologous blood donation by the attending surgeon or cardiologist. To our knowledge the referring surgeons and cardiologists did not select or exclude patients from participation in the autologous program on the basis of any criteria. Each referral for autologous services was made in writing. The median number of requested donations was 2 units. This equals the median blood support required for aortic valve replacement in our institutions. The predonation history, limited physical examination, and hematocrit testing were the same as that done for all other autologous donors in our autologous blood programs. Any suggestion of potential complication from blood donation was investigated by a transfusion medicine physician. Details were elicited about complications during previous episodes of volume depletion, pattern of angina pectoris, history of arrhythmias, and current medications. Results of cardiac catheterization were not used to assess donor suitability. Each patient was counseled about the risks of donation in the setting of aortic valve disease and gave written informed consent for the procedure.

Accepted for publication April 10, 1992.

Address reprint requests to Dr Dzik, Blood Bank and Tissue Typing Laboratory, New England Deaconess Hospital, 185 Pilgrim Rd, Boston, MA 02215.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

During the blood donation, supplemental oxygen and electrocardiographic monitoring were available but not used. Blood collection was performed according to standards established by the American Association of Blood Banks. A criterion for acceptance was a predonation hematocrit greater than or equal to 0.33. Blood was collected into citrate-phosphate-dextrose-adenine anticoagulant preservative bags 35 to 3 days before the scheduled operation and stored as whole blood (WB). The procedure used for the collection resulted in the removal of a mean of 475 mL of WB in less than 10 minutes.

During each operation blood was salvaged from the operative field and from the pump-oxygenator. Transfusions were administered according to the assessment of the surgeons and anesthesiologists. No unusual effort was made to restrict the use of homologous blood. Records of blood use were obtained from each transfusion service. Transfusion requirements of the 79 study patients (autologous group) were compared with those of 298 patients (nonautologous group) who underwent elective aortic valve replacement during the same time period without autologous blood donation. The proportion of patients exposed to homologous blood was determined. Because blood component use during operation follows a non-Gaussian distribution, the proportion of patients transfused and the median and range of blood use for both groups were determined. Statistical significance of the difference in blood use between the two groups was determined by the χ^2 test.

Results

A total of 79 consecutive patients were referred to the program, and all were able to donate. No patient was excluded on the basis of predonation history or physical. Clinical characteristics of the population are shown in Table 1 and are representative of patients requiring aortic valve replacement in our institutions. Each patient had New York Heart Association functional class III or IV cardiac symptoms. In addition, some patients gave a history of previous episodes of syncope with loss of consciousness or prior myocardial infarction. All patients, except 1, were taking a variety of prescribed medicines in various combinations. These medicines included digoxin, diuretics, angiotensin converting enzyme inhibitors, calcium-channel blockers, β-blockers, nitrates, anticoagulants, oral hypoglycemics, and antibiotics.

A total of 129 units of WB were collected from the 79 patients with a median of 2 units (range, 1 to 3 units) per donor. Two patients donated but were unable to complete their prescribed number of donations owing to a low hemoglobin concentration. During the donations there was one complication that may have been related to preoperative blood collection. The patient, a 74-year-old man with a history of exertional syncope, suffered a syncopal episode outside of the hospital approximately 2 hours after donation after walking 0.8 km up a gradual incline. He was admitted to the hospital for observation and discharged the next day.

Aortic valve replacement was performed on 78 patients. Twenty of these had simultaneous coronary artery bypass grafting (median, 2 grafts; range, 1 to 5 grafts). One patient's operation was canceled. Three operations were postponed due to intercurrent illness. The autologous blood of these patients became outdated and none of them gave additional preoperative autologous donations. The blood use of the three patients with postponed operations is included in the study group.

Exposure to donor blood for the 78 patients who came to operation is shown in Table 2. Among those who donated autologous blood, 4 patients (5%) required no transfusions whatsoever during their hospitalizations. Of particular note, 49 patients (63%) received only autologous blood during their entire hospitalization. Thus, only

Table 1. Clinical Features of 79 Autologous Blood Donors Before Aortic Valve Replacement

Feature	
Age (y)	
Median	64
Range	19–76
Male/female	59/20
Valve lesions	
Pure AS	31 (39%)
Mixed AS/AI	37 (47%)
Pure AI	11 (14%)
Symptoms (%)	
Shortness of breath	75
Dizziness	51
Angina pectoris	31
Syncope	13
AVA (cm²)	
Median	0.7
Range	0.2–1.2
Mean[a] pressure gradient (mm Hg)	63 ± 24
Patients requiring CABG	20
Mean[a] hematocrit	
Preop	0.38 ± 0.05
Discharge	0.30 ± 0.05

AI = aortic insufficiency; AS = aortic stenosis; AVA = aortic valve area among patients with aortic stenosis; CABG = coronary artery bypass grafting.

[a] Mean ± standard deviation.

Table 2. Blood Donor Exposures During Aortic Valve Replacement[a]

Donor Exposures	Autologous Group (n = 78)	Nonautologous Group (n = 298)
No transfusions	4 (5)[b]	91 (31)
Autologous only	49 (63)[b]	. . .
1–2 homologous unit	12 (15)	76 (25)
3–10 homologous units	7 (9)	83 (28)
>10 homologous units	6 (8)	48 (16)

[a] The number of patients exposed to donor blood components (exposure to all components including whole blood, packed red cells, fresh frozen plasma, platelets and cryoprecipitate during entire hospitalization) is shown. Values in parentheses are percentages. [b] Proportion of patients with either no transfusion exposures or autologous only transfusions is significantly different from nonautologous group ($p < 0.0001$).

Table 3. Blood Component Use for Patients Undergoing Elective Aortic Valve Replacement

Component	Autologous Group (n = 78)	Non-autologous Group (n = 298)	p Value
For all patients, median number of units transfused per patient			
WB	1	0	
Packed RBCs	0	2	
Combined WB + RBCs	2	2	
FFP	0	0	
Platelets	0	0	
Percentage of patients transfused			
WB	91	3	<0.00001
Packed RBCs	27	65	<0.00001
Combined WB + RBCs	95	66	<0.0001
FFP	17	27	NS
Platelets	6	16	<0.05
For transfused patients, median (range) units transfused per patient			
WB	1 (1–14)	2 (1–2)	
Packed RBCs	2 (1–58)	3 (1–51)	
Combined WB + RBCs	2 (1–72)	3 (1–51)	
FFP	4 (1–42)	4 (1–33)	
Platelets	10 (6–41)	6 (5–54)	

FFP = fresh frozen plasma; NS = not statistically significant; RBCs = red blood cells; WB = whole blood.

32% of patients who predonated blood were exposed to any homologous blood. In contrast, during the same period, 298 other patients underwent aortic valve replacement without preoperative autologous blood collections and 69% were transfused with homologous blood. When the two groups were compared, a significantly greater proportion of patients who donated autologous blood avoided exposure to any homologous blood products ($p <$ 0.0001).

Component therapy for the 78 patients is shown in Table 3. Patients who predeposited their own blood received chiefly autologous WB, whereas those who did not predeposit received chiefly packed red blood cells. When these two forms of red cell support were considered together, it was found that both the autologous group and the nonautologous group each received a median of 2 red cell products per patient. The median number of other components transfused per patient for the two groups was zero. The proportion of patients in the two groups transfused with fresh frozen plasma was not significantly different, but a higher proportion of patients who did not predeposit blood were transfused with platelets.

Comment

Aortic stenosis has been considered a contraindication to preoperative autologous blood donation [2, 3]. Although two recent national studies found that preoperative autologous blood donation is a safe procedure, patients with aortic valve disease were excluded from participation [4, 5]. Even programs that routinely collect autologous blood before coronary revascularization have excluded patients with aortic valve disease [6]. Thus, published reports of preoperative autologous blood donation by patients awaiting cardiac operations include only a limited number of individuals with aortic valve lesions [7, 8]. However, one report described a single institution's experience with a heterogeneous population of "high-risk" donors [9]. Among them were 63 patients with a variety of valvular heart conditions. Only one of their 63 patients experienced a serious donor reaction (fainting). The number of patients with aortic valve disease and the severity of the aortic valve disease is not stated in their report, nor is the efficacy of the procedure for avoiding homologous donor exposures.

In our experience preoperative blood donation before elective aortic valve replacement appears to be both safe and effective. Only one patient suffered a reaction that may have been related to donation. A significantly lower percentage of patients who gave autologous blood were exposed to homologous donors at the time of operation. Although patients were not randomly assigned to the autologous and nonautologous groups, overall blood component therapy for the two groups was comparable, suggesting that the two groups were similar in surgical complexity. Both groups received a median of 2 units of red cell support per patient. This was provided by predonated blood in the autologous group and by homologous blood in the nonautologous group. The proportion of patients requiring more than 10 components was not different in the two groups. The proportion of patients requiring supplemental fresh frozen plasma and the median number of units of fresh frozen plasma required were not different, suggesting that the use of autologous WB did not influence the decision to transfuse fresh frozen plasma. Although platelet transfusions were given to only a minority of patients, it is interesting that a slightly smaller proportion of patients receiving autologous WB were transfused with platelet concentrates ($p <$ 0.05; see Table 3). Whether or not the decreased use of platelets in the autologous group was due to a beneficial hemostatic effect of WB cannot be concluded from our data.

It is noteworthy that only 5% of patients in the autologous group were not transfused (did not receive even their own blood) compared with 31% of patients in the nonautologous group ($p < 0.001$; see Table 2). Two explanations seem plausible to account for this significant difference. First, surgeons and anesthesiologists may have felt less reluctant to transfuse autologous blood than homologous blood given the lower risk of the former. Indeed, separate "transfusion triggers" for autologous and homologous blood are a logical consequence of risk/benefit analysis of the decision to transfuse. Second, a greater proportion of patients who preoperatively donated autologous blood may have entered operation at a lower hematocrit and thus may have required red cell replacement. Our data do not permit us to determine which explanation accounts for the observed difference in transfusion therapy. However, a similar difference in the proportion of transfused individuals among patients with and without available autologous blood has been noted in a national multicenter study [10].

It has been suggested that patients with aortic valve disease should be given saline solution at the time of autologous donation (isovolemic donation) [11]. We did not routinely use saline solution in our patients, but did infuse saline solution in 6 of 30 donations (20%) at one program (Deaconess Hospital, Boston, MA). Patients were not randomly assigned to receive saline solution, and we cannot comment on the utility of this procedure for autologous donation. There are no specific studies documenting the utility of isovolemic donation. Of note, saline solution was not used by the other participating program (Hudson Valley Blood Services, Valhalla, NY) and is not routinely used in the large experience with high-risk autologous donations at the Cedars-Sinai Medical Center in Los Angeles, CA (Dennis Goldfinger, MD, personal communication).

The expansion in autologous blood services for patients undergoing cardiopulmonary bypass is likely to continue. Studies are currently underway to evaluate the clinical effectiveness of erythropoietin [12] and of preoperative [13] or intraoperative [14] collection of autologous platelet-rich plasma before cardiopulmonary bypass. As the risk of homologous blood changes, the utility of autologous blood techniques will also change [15], and decisions regarding which patients should receive autologous blood services will require reevaluation. In contrast to prevailing opinion, our experience serves to document that preoperative autologous blood collection not only is effective but also is safe for patients with aortic valve disease. A significantly higher proportion of patients undergoing aortic valve replacement were able to avoid homologous donor exposures as a result of participating in a preoperative autologous blood donation program. The rate of donation reactions for our study group (0.8%) compares favorably with published rates of "low-risk" autologous or routine volunteer blood donations (2% to 4%) [4, 5]. Our donors had too few reactions for us to judge whether or not the morbidity of a donation reaction would be substantially greater in patients with aortic valve disease. Concern over this point may persuade some to restrict blood collections from patients awaiting aortic valve operations to a hospital-based blood donation program. Nevertheless, our experience suggests that the option of preoperative autologous blood donation should be considered for patients awaiting elective aortic valve replacement.

We express our appreciation to the staff of the Hudson Valley Blood Services and the New England Deaconess Hospital Blood Bank for the expert care given to the patients who participated in this study.

References

1. Chambers LA, Kruskall MS. Preoperative autologous blood donation. Trans Med Rev 1990;4:35–46.
2. Gianino NJ. Special procedures. In: Green TS, Steckler D, eds. Donor room policies and procedures. Arlington, VA: American Association of Blood Banks, 1985:49.
3. Sayers MH. Autologous blood donation by cardiac surgery patients: wisdom or folly? In: Maffei LM, Thurer RL, eds. Autologous blood transfusion: current issues. Arlington, VA: American Association of Blood Banks, 1988:111–7.
4. Aubuchon JP, Popovsky MA. The safety of preoperative autologous blood donation in the nonhospital setting. Transfusion 1991;31:513–7.
5. McVay PA, Andrews A, Kaplan EB, et al. Donation reactions among autologous donors. Transfusion 1990;30:249–52.
6. Owings DV, Kruskall MS, Thurer RL, Donovan LM. Autologous blood donations prior to elective cardiac surgery: safety and effect on subsequent blood use. JAMA 1989;262:1963–8.
7. Britton LW, Eastlund T, Dziuban SW, et al. Predonated autologous blood use in elective cardiac surgery. Ann Thorac Surg 1989;47:529–32.
8. Love TR, Hendren WG, O'Keefe DD, Daggett WM. Transfusion of predonated autologous blood in elective cardiac surgery. Ann Thorac Surg 1987;43:508–12.
9. Mann M, Sacks HJ, Goldfinger D. Safety of autologous blood donation prior to elective surgery for a variety of potentially "high risk" patients. Transfusion 1983;23:229–32.
10. Toy PTCY, Strauss RG, Stehling LC, et al. Predeposited autologous blood for elective surgery: a national multicenter study. N Engl J Med 1987;316:517–20.
11. Sassetti R, Spiess B, McLeod B, Narbone R. Hemodynamic changes in high risk autologous donors [Abstract]. Transfusion 1988;28:34S.
12. Watanabe Y, Fuse K, Konishi T, et al. Autologous blood transfusions with recombinant human erythropoietin in heart operations. Ann Thorac Surg 1991;51:767–72.
13. Noon GP, Jones J, Fehir K, Yawn DH. Use of pre-operatively obtained platelets and plasma in patients undergoing cardiopulmonary bypass. J Clin Apheresis 1990;5:91–6.
14. Giordano GF, Rivers SL, Chung GKT, et al. Autologous platelet-rich plasma in cardiac surgery: effect on intraoperative and postoperative transfusion requirements. Ann Thorac Surg 1988;46:416–9.
15. Dzik WH, Devarajan S. Should autologous blood from infectious donors be used or discarded: a decision analysis approach. Transfusion 1989;29:743–5.

INVITED COMMENTARY

This investigation demonstrates the safety and efficacy of preoperative autologous blood donation in a subgroup of 20% of those patients having elective aortic valve replacement at the participating centers during the study period. Although the data presented seem favorable, the applicability of the technique to the overall group is unclear. Although Dzik and associates argue that the study group is representative in terms of surgical complexity, we are not given information such as age, male/female ratio, and the extent of coronary disease in the control patients to allow us to assess the potential risks of donation for the group as a whole. Contrary to Dzik and associates' assertion, the referring surgeons and cardiologists may have been quite selective in their referrals for blood donation.

This study challenges the "conventional wisdom" of excluding patients with aortic stenosis from blood donation. However, when one considers the ever-improving safety of homologous blood transfusion and the risks associated with both the donation process and the attendant delay in operation, I believe further data are needed before preoperative autologous blood donation is routinely offered to patients with severe aortic valve disease.

Robert L. Thurer, MD

Division of Cardiothoracic Surgery
Beth Israel Hospital
330 Brookline Ave
Boston, MA 02215

Notice From The Society of Thoracic Surgeons

The Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons will be held at the San Antonio Convention Facility in San Antonio, Texas, January 25–27, 1993. There is no registration fee for the meeting for members of The Society. The registration fee is also waived for speakers, residents, and fellows. A $250.00 guest registration fee will apply to all other nonmember physicians.

The Twenty-sixth Postgraduate Course is scheduled for Sunday, January 24, 1993. The registration fee is $65.00 for all attendees. The Postgraduate Program will include minisymposia dealing with Thoracoscopy, Current Pulmonary Surgical Problems, Decisions in Cardiac Surgery, and Transplantation. A C.C.C.E.T.S. Basic Science Lecture and a special luncheon presentation by Floyd Loop on a subject of general interest will also be included.

In addition to the Postgraduate Program, this year's Annual Meeting will include a scientific poster session, breakfast seminars, the annual movie night, a wide range of surgical exhibits, and a complete schedule of scientific presentations drawn from the largest volume of abstracts ever submitted for presentation to The Society.

An advance program information booklet will be mailed to all members of The Society this fall. It will include a detailed schedule of events as well as registration and housing forms and other pertinent information regarding the Annual Meeting. Nonmembers wishing to receive the advance program booklet should write to the Secretary of The Society, Richard P. Anderson, MD.

Richard P. Anderson, MD
Secretary
The Society of Thoracic Surgeons
401 N Michigan Avenue
Chicago, IL 60611
(312) 644-6610
FAX (312) 527-6635

Clinical and Hemodynamic Evaluation of the 19-mm Carpentier-Edwards Supraannular Aortic Valve

Panny Kallis, FRCS, James F. Sneddon, MRCP, Iain A. Simpson, MRCP,
Anthony Fung, FRCS, John R. Pepper, FRCS, and E. E. John Smith, FRCS

Departments of Cardiothoracic Surgery and Cardiology, St. George's Hospital, London, England

The clinical and hemodynamic performance of the 19-mm Carpentier-Edwards supraannular aortic valve is largely unknown compared with that of the larger valves. Over 4 years we implanted the 19-mm Carpentier-Edwards supraannular aortic valve into 21 patients (20 female) with a mean age of 75 ± 1.2 years (range, 59 to 86 years) and a mean body surface area of 1.6 ± 0.03 m^2 (range, 1.3 to 1.7 m^2). There were four deaths, one operative and three late noncardiac deaths. Follow-up of the 17 survivors for a mean of 20 ± 3.1 months (range, 2 to 42 months) demonstrated symptomatic improvement in all 17 (all are now in New York Heart Association functional class I or II). There were no valve-related complications and no patient required long-term anticoagulation. Doppler echocardiographic studies were used to assess the in vivo hemodynamic profile of the valve. Mean postoperative aortic valve gradient was 34.1 ± 2.7 mm Hg (range, 19 to 52 mm Hg). Functional valve orifice area was 1.1 ± 0.09 cm^2 (range, 0.6 to 1.8 cm^2). Mean cardiac output was 3.92 ± 0.17 L/min (range, 3.2 to 5.1 L/min) with a mean cardiac index of 2.5 ± 0.11 $L \cdot min^{-1} \cdot m^{-2}$ (range, 2.1 to 3.2 $L \cdot min^{-1} \cdot m^{-2}$). In conclusion, we have demonstrated that aortic valve replacement with the 19-mm Carpentier-Edwards supraannular aortic valve has a low operative mortality and offers major clinical benefits despite moderate transprosthetic gradients. This approach provides an alternative management strategy in elderly patients who would otherwise require low-profile mechanical valves or aortic root enlargement.

(Ann Thorac Surg 1992;54:1182–5)

Valves larger than 21 mm have good hemodynamic performance, unlike many of the 19-mm valves. The 19-mm Björk-Shiley [1, 2] and the 19-mm St. Jude Medical [2, 3] valves have low transprosthetic gradients but require long-term anticoagulation. Of the 19-mm tissue valves only the Ionescu-Shiley pericardial valve has been shown to have adequate hemodynamics, but this has been withdrawn because of unacceptable failure rates [4, 5].

The in vivo hemodynamic performance of the 19-mm Carpentier-Edwards supraannular porcine aortic valve (CE-SAV) (Baxter-Edwards, Irvine, CA) is largely unknown. There has been reluctance to implant this valve because of the potential adverse hemodynamic profile associated with the use of such small diameters. Aortic valve replacement (AVR) with a 19-mm valve in a patient with body surface area larger than 1.7 m^2 and good cardiac output can result in high transvalvular gradients (valve–patient mismatch) and prevent clinical improvement of the patient [6]. Surgeons have therefore tended to either use a low-profile mechanical valve or enlarge the aortic annulus.

The small aortic root, however, is frequently encountered in elderly patients, mainly women, in whom anticoagulation is undesirable and aortic root enlargement might increase the morbidity and mortality [1]. For these reasons the 19-mm CE-SAV was our bioprosthetic valve of choice for this population between 1986 and 1991.

This report of clinical follow-up and postoperative two-dimensional Doppler echocardiographic assessment defines the normal in vivo hemodynamic profile of the 19-mm CE-SAV and identifies the group of patients in whom a small valve can provide an acceptable clinical result.

Material and Methods

Patient Population

The hemodynamic profile and clinical outcome of 21 consecutive patients who underwent AVR with the 19-mm CE-SAV were reviewed. Demographic data showed 1 male and 20 female patients with a mean age of 75 ± 1.2 years (range, 59 to 86 years). The mean body surface area was 1.6 ± 0.03 m^2, with a range of 1.3 to 1.7 m^2.

The main presenting symptoms were shortness of breath on exertion (17), angina (9), syncope (4), and pulmonary edema (1), with 10 patients having more than one symptom. Twenty patients underwent preoperative cardiac catheterization with an average aortic gradient of 96 ± 6.4 mm Hg (range, 50 to 140 mm Hg). One patient, who presented with pulmonary edema, had the diagnosis

---

Accepted for publication April 13, 1992.

Address reprint requests to Mr Kallis, Department of Cardiothoracic Surgery, Harefield Hospital, Harefield, Middlesex UB9 6JH, England.

© 1992 by The Society of Thoracic Surgeons 0003-4975/92/$5.00

of aortic stenosis confirmed on the basis of echocardiography alone, as she required an emergency operation. One patient had undergone an unsuccessful balloon valvuloplasty.

Thirteen of the procedures were classified as urgent, seven as elective, and one as an emergency. Four of the patients were classified as being in New York Heart Association (NYHA) functional class IV, 12 in class III, and 5 in class II preoperatively. Isolated AVR was performed in 15 patients, AVR and concomitant coronary revascularization in 5 patients, and AVR and mitral valve replacement in 1 patient.

Operative Technique

All patients received prophylactic intravenous cefuroxime at the time of induction of anesthesia, and this antibiotic regimen was continued for 48 hours postoperatively. Venous drainage was achieved with a two-stage cannula (Stockert-Shiley, Irvine, CA); a membrane oxygenator was used, and the return was into the distal ascending aorta (26F to 28F Wessex cannula). Cardiopulmonary bypass was established with systemic hypothermia to 25°C with flow rates of 1.6 to 2.4 $L \cdot min^{-1} \cdot m^{-2}$ and a mean arterial pressure of 60 mm Hg. A vent was placed through the apex of the left ventricle. Multidose cold crystalloid cardioplegia (St. Thomas' solution) was infused directly into the coronary ostia. Topical cooling was also used (4°C Hartmann's solution). After excision of the valve, the aortic annulus was debrided of residual calcium and the 19-mm CE-SAV was placed in the supraannular position with interrupted sutures of 2-0 Ticron (Davis & Geck, Gosport, Hampshire, England). No anticoagulants were used postoperatively in patients who underwent isolated AVR, but aspirin was used in patients who underwent concomitant coronary revascularization. Warfarin was used in the patient who underwent additional mitral valve replacement, but this was discontinued after 2 months.

Clinical Follow-up

Postoperative complications were determined from patient records. Fifteen of the 17 survivors were reviewed in the outpatient clinic at the time of the study for recurrent symptoms, NYHA functional status, medications being taken, and valve-related complications. The remaining 2 survivors who were unable to attend because of distance were assessed over the telephone. The causes of late deaths were determined from the patient records and postmortem reports.

Echocardiographic Follow-up

Two-dimensional echocardiography and Doppler ultrasound were performed (parasternal and apical views) using a Vingmed CFM 750 with a 3.5-MHz transducer. The maximum velocity (V) through the aortic prosthesis measured by continuous-wave Doppler ultrasound was used to estimate the aortic valve gradient at rest using the modified Bernoulli equation [7]: maximum instantaneous gradient = $4V^2$.

Two-dimensional echocardiography was used to measure the diameter of the left ventricular outflow tract (LVOT) from the parasternal long-axis view, and pulsed-wave Doppler ultrasound from the apex was used to determine the left ventricular outflow tract velocity. Aortic valve (AV) area was then calculated using the equation of continuity [8] such that: area(LVOT) × velocity(LVOT) = area(AV) × velocity(AV). The cardiac output at rest was calculated using the formula [9]: cardiac output = time velocity integral × AV area × heart rate.

Statistical Analysis

All data are expressed as the mean ± the standard error of the mean using the statistical package Clinstat.

Results

Early Morbidity and Mortality

There was one operative death (4.8%) in a 79-year-old woman (NYHA class IV) who underwent AVR and triple coronary artery bypass grafting. She also had moderate mitral regurgitation, but the mitral valve was not replaced. One patient, who had pulmonary edema preoperatively, required the use of inotropic agents and an intraaortic balloon to come off bypass. Three patients (14%) underwent resternotomy for bleeding secondary to coagulopathy, and acute renal failure developed in 1 patient (4.8%). Two patients (9.5%) required placement of a permanent pacemaker system because of complete heart block postoperatively. One patient underwent a tracheostomy for prolonged ventilation.

Late Clinical Follow-up

There were three late deaths: at 2 months due to a gangrenous leg in an 80-year-old diabetic woman, at 15 months due to a blocked tracheostomy, and at 24 months due to hepatic metastases.

All 17 of the survivors were traced (by April 1991). Mean follow-up was 20 ± 3.1 months (range, 2 to 42 months). Fifteen of these patients were interviewed and examined, whereas 2 were interviewed over the telephone because of distance. There were no valve-related complications such as thromboembolic events, prosthetic endocarditis, hemolysis, or aortic insufficiency requiring reoperation. No patient required long-term anticoagulation, and none of them suffered any gastrointestinal hemorrhage.

All the survivors were on less medication than preoperatively, and they all demonstrated excellent clinical improvement according to the NYHA functional classification (Fig 1). Two (11.8%) were in class IV, 11 (64.7%) in class III, and 4 (23.5%) in class II preoperatively, whereas 7 (41.2%) were in class II and 10 (58.8%) in class I postoperatively. Every patient had improved NYHA functional status.

Echocardiographic Follow-up

Fifteen of the 17 patients had postoperative echocardiograms at the time of the study (average time, 20 ± 3.1 months; range, 2 to 42 months). In 1 patient it was impossible to obtain an adequate Doppler signal to calcu-

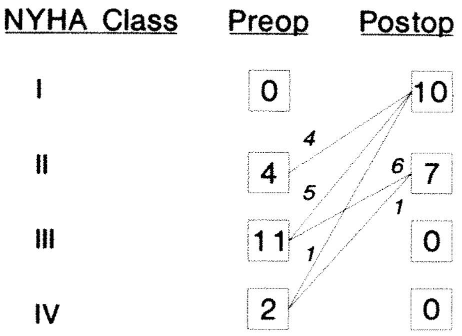


Fig 1. Comparison of the New York Heart Association (NYHA) functional status of the 17 survivors preoperatively and postoperatively (time of follow-up).

late the transprosthetic gradient and valve area. The two-dimensional echocardiogram demonstrated hypertrophy of the left ventricle and good left ventricular function in the other 14 patients. There was no evidence of structural failure of any of the prostheses, but there was a minor paraprosthetic leak in 1 patient. This was not significant hemodynamically, however, as the patient was in NYHA functional class I.

The mean cardiac output at rest was 3.92 ± 0.17 L/min (range, 3.2 to 5.1 L/min) with a cardiac index of 2.5 ± 0.11 L · min^{-1} · m^{-2} (range, 2.1 to 3.2 L · min^{-1} · m^{-2}), which is at the lower end of the normal range for 75-year-olds. The average maximum instantaneous gradient at rest was 34.1 ± 2.7 mm Hg (range, 19 to 52 mm Hg). The mean effective valve area was 1.1 ± 0.09 cm^2 (range, 0.6 to 1.8 cm^2).

Comment

Aortic valve replacement in the small aortic root presents a special challenge to the surgeon in regard to both operative technique and selection of prosthesis. These patients are predominantly older women with small body surface areas and severe calcific aortic stenosis, as confirmed by our patient population.

When choosing a prosthesis for these patients three main factors have to be considered. First, such patients are unable to withstand difficult and prolonged procedures, which carry a high mortality and morbidity [1, 10]. Second, the hemodynamic performance of the prosthesis chosen must be adequate to avoid valve prosthesis–patient mismatch, which would prevent clinical improvement of the patient [6]. Third, use of anticoagulants in elderly patients should be avoided if possible.

Enlarging the aortic annulus, either with an incision through the annulus into the anterior mitral leaflet [10] or with a more extensive aortoventriculoplasty (Konno procedure) [11], is poorly tolerated in elderly patients with calcified aortic roots [12].

The small Starr-Edwards valves (7-A and 8-A) have unacceptable transprosthetic gradients and are associated with an increased perioperative mortality [13]. Catheterization data of patients with 19-mm St. Jude valves showed a peak-to-peak gradient of 16 mm Hg and functional orifice area of 1.22 cm^2 [3]. Echocardiographic assessment of the same valve showed a maximum instantaneous gradient of 38 mm Hg [14].

Catheterization of patients with a 19-mm Björk-Shiley valve revealed a functional orifice area of 1.06 cm^2 and a peak systolic gradient of 16 mm Hg [1]. Major bleeding complications occurred in 13% of these patients, and minor bleeding complications developed in a further 13% [1].

The main advantage of tissue valves is the avoidance of anticoagulants, but structural failure still remains a problem. Bojar and colleagues [4] reported a good hemodynamic profile of the 19-mm Ionescu-Shiley pericardial valve echocardiographically. The maximum instantaneous gradient was 17 mm Hg and the effective orifice area 1.2 cm^2. They also confirmed low operative mortality and demonstrated excellent clinical improvement, but the valve was withdrawn from the market in 1987 because of unacceptable structural failure rates.

The 19-mm modified Hancock valve has a peak systolic gradient of 22 mm Hg and a functional orifice area of 1.1 cm^2 [2]. The standard Carpentier-Edwards prosthesis has a smaller width of the prosthetic base and an asymmetric annulus, which provides a more effective orifice to external diameter ratio. In vivo hemodynamic data of the 19-mm valve, however, are scarce. Catheterization data in 3 patients revealed a peak systolic gradient of 33 mm Hg and a functional orifice area of 1.1 cm^2 [15].

Carpentier and colleagues [16] described the design and preservation techniques of the CE-SAV in 1982. The prosthesis was developed to be implanted in the supraannular position, rather than within the annulus, to provide an orifice of the same diameter as the patient's annulus. Such an approach attempted to reduce the transvalvular gradient across the standard 19-mm valve.

The in vivo hemodynamic performance of the 19-mm CE-SAV is largely unknown because of fear of unacceptable transprosthetic gradients and failure of clinical improvement of the patient. This study, however, demonstrates that AVR with a 19-mm CE-SAV leads to major symptomatic improvement of the patients despite moderate transprosthetic gradients. As seen in the scattergram in Figure 2 there was no correlation between transprosthetic gradient and body surface area. The higher gradients are therefore more likely to be due to variation of cardiac output than to valve prosthesis–patient mismatch. Foster and colleagues [2] also found that there was no correlation of transvalvular gradient at rest with the clinical status of the patients at follow-up. Continuous-wave Doppler ultrasound estimates the maximum instantaneous gradient rather than the peak-to-peak gradient as measured at cardiac catheterization. The more physiological Doppler-defined gradient, therefore, may be as much as 20 mm Hg higher than the peak-to-peak gradient [17, 18].

Jamieson and colleagues [19] in 1988 reported their overall clinical results in 1,167 patients in whom they implanted CE-SAVs of all sizes. The freedom from structural deterioration at 4 years was 99% and from all

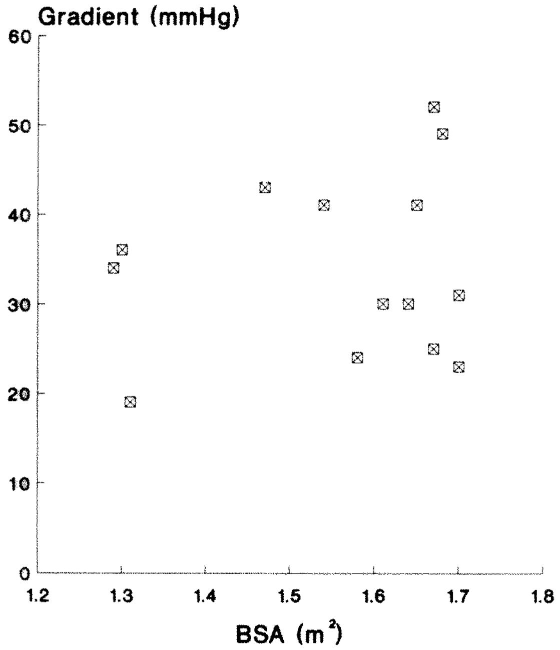


Fig 2. Scattergram of maximum instantaneous gradient and body surface area (BSA), showing no correlation (r = 0.15).

valve-related complications, 86%. They therefore concluded that the CE-SAV offers excellent intermediate clinical results.

In conclusion, this study defines the normal in vivo hemodynamic profile of the 19-mm CE-SAV. It also demonstrates that its use is associated with low operative mortality and low incidence of valve-related complications, and offers major clinical improvement despite moderate transprosthetic gradients. We believe that this approach provides an alternative management strategy in the small elderly patients who would otherwise require a low-profile mechanical valve or enlargement of the aortic annulus.

References

1. Schaff HV, Borkon AM, Hughes C, et al. Clinical and hemodynamic evaluation of the 19 mm Björk-Shiley aortic valve prosthesis. Ann Thorac Surg 1981;32:50–7.
2. Foster AH, Tracey CM, Greenberg GJ, McIntosh CL, Clark RE. Valve replacement in narrow aortic roots: serial hemodynamics and long-term clinical outcome. Ann Thorac Surg 1986;42:506–16.
3. Wortham DC, Tri TB, Bowen TE. Hemodynamic evaluation of the St. Jude Medical valve prosthesis in the small aortic annulus. J Thorac Cardiovasc Surg 1981;81:615–20.
4. Bojar RM, Diehl JT, Moten M, et al. Clinical and hemodynamic performance of the Ionescu-Shiley valve in the small aortic root. J Thorac Cardiovasc Surg 1989;89:1087–95.
5. Revuelta JM, Duran CMG, Garcia-Rinaldi R. Performance of the Ionescu-Shiley pericardial valve in the small aortic annulus. In: Proceedings of the cardiac prosthesis symposium III, September 1985. Montreux, Switzerland: Shiley, Inc, 1987: 17–22.
6. Rahimtoola SH. The problem of valve prosthesis–patient mismatch. Circulation 1978;58:20–4.
7. Simpson IA, Houston AB, Sheldon CD, Hutton I, Lawrie TDV. Clinical value of Doppler echocardiography in the assessment of adults with aortic stenosis. Br Heart J 1985;53: 636–9.
8. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. Circulation 1985;72:810–8.
9. Huntsman LL, Stewart DK, Barnes SR, Franklin SB, Colocousis JS, Hessel EA. Noninvasive Doppler determination of cardiac output in man. Clinical validation. Circulation 1983; 67:593–602.
10. Manouguian S, Seybold-Epting W. Patch enlargement of the aortic valve ring by extending the aortic incision into the anterior mitral leaflet: new operative technique. J Thorac Cardiovasc Surg 1979;78:402–12.
11. Misbach GA, Turley K, Ullyot DJ, Ebert PA. Left ventricular outflow enlargement by the Konno procedure. J Thorac Cardiovasc Surg 1982;84:696–703.
12. Rastan H, Abu-Aishah N, Rastan D, et al. Results of aortoventriculoplasty in 21 consecutive patients with left ventricular outflow tract obstruction. J Thorac Cardiovasc Surg 1978;75:659–69.
13. Blank RH, Pupello DF, Bessone LN, Harrison EE, Sbar S. Method of managing the small aortic annulus during valve replacement. Ann Thorac Surg 1976;22:356–61.
14. Panidis IP, Ross JR, Mintz GS. Normal and abnormal prosthetic valve function as assessed by Doppler echocardiography. J Am Coll Cardiol 1986;8:317–26.
15. Bove EL, Marvasti MA, Potts JL, et al. Rest and exercise hemodynamics following aortic valve replacement: a comparison between 19 and 21 mm Ionescu-Shiley pericardial and Carpentier-Edwards porcine valves. J Thorac Cardiovasc Surg 1985;90:750–5.
16. Carpentier A, Dubost C, Lane E, et al. Continuing improvement in valvular prostheses. J Thorac Cardiovasc Surg 1982; 83:27–42.
17. Cooper DM, Stewart WJ, Schiavone WA, et al. Evaluation of normal prosthetic valve function by Doppler echocardiography. Am Heart J 1987;114:576–82.
18. Reisner SA, Meltzer RS. Normal values for prosthetic valve Doppler echocardiographic parameters: a review. J Am Soc Echocardiogr 1988;1:200–10.
19. Jamieson WRE, Munro AI, Miyagishima RT. The Carpentier-Edwards supraannular porcine bioprosthesis. A new generation of tissue valve with excellent intermediate clinical performance. J Thorac Cardiovasc Surg 1988;96:652–66.

Optimal Approach to the Mitral Valve: Dissection of the Interatrial Groove

Robert I. Larbalestier, MD, Richard B. Chard, FRCS, and Lawrence H. Cohn, MD

Department of Surgery, Harvard Medical School, and Division of Cardiac Surgery, Brigham and Women's Hospital, Boston, Massachusetts

Surgical exposure of the mitral valve has challenged surgeons for more than 30 years. Many ingenious, but often complex approaches have been devised during this time. Using the dissection of the interatrial groove to bring the left atrial incision more anterior and medial, we have achieved excellent exposure in more than 300 mitral valve procedures. This simple technique does not lengthen the procedure and is not associated with an increased risk of either early or late morbidity.

(Ann Thorac Surg 1992;54:1186–8)

The increasing population of patients requiring mitral repair procedures, mitral reoperations, or procedures in small left atria has made it clear to surgeons interested in these procedures that successful operations require excellent exposure of the whole mitral apparatus and all left atrial structures. Many surgeons find adequate exposure difficult, making mitral valve procedures unnecessarily lengthy. As a consequence the recent surgical literature has contained many articles [1–8] describing various techniques allowing improved exposure of the mitral valve. We describe our routine technique for mitral valve exposure incorporating dissection of the interatrial groove, which is based on Sondergaard and associates' [9] early work on closed techniques of repair of atrial septal defects.

Material and Methods

For all primary and first time reoperations we prefer to expose the heart and great vessels through the usual median sternotomy incision. Cardiopulmonary bypass is then established using an ascending aortic cannula and bicaval cannulation for venous return. Cardioplegia is delivered through the ascending aorta after cross-clamping and is repeated every 20 minutes.

In patients undergoing a third or greater reoperation we use a right thoracotomy incision [10] if there is no major aortic regurgitation and no requirement for associated coronary artery bypass grafting. In this approach we retract the lung and divide the pericardium anterior to the phrenic nerve to expose the lateral walls of the atria in front of the pulmonary veins. Bypass is established in this situation by exposure of the femoral vessels and the use of the long percutaneous Bio-Medicus (Eden Prairie, MN) cannulas [11].

The most common approach to the mitral valve is through an incision commencing in front of the right superior pulmonary vein and running parallel to the interatrial groove [12, 13]. We differ from this by taking advantage of the extensive infolding of tissue between the right superior pulmonary vein and the venous sinus of the atrium. These walls join to form the septum secundum component of the atrial septum, which is the superior limbus of the fossa ovalis [14]. This infolding of tissue forms the interatrial groove. Dissection of this plane was first described by Sondergaard and associates [9] in 1955, in their article on repair of atrial septal defects. It lies between the sulcus terminalis and the right pulmonary veins and is filled with a variable amount of fat [14] (Fig 1).

Development of this plane is achieved by a combination of sharp and blunt dissection reflecting the right atrium anteriorly (Fig 2). The most medial and anterior aspect of the left atrium is exposed just adjacent to the interatrial septum (Fig 3). Incision into the left atrium is then made parallel to the right pulmonary veins but is now 4 to 6 cm closer to the mitral valve (Figs 4, 5).

Extension of this incision can be achieved superiorly into the roof of the atrium in the transverse sinus and inferiorly into the inferior wall of the atrium in the oblique sinus after simple mobilization and retraction of both cavae anteriorly.

We use a number of other maneuvers to assist exposure in the difficult case. Anterior suspension of the right-sided pericardial flap with detachment of the leftward pericardium from the back of the sternum allows anterior and

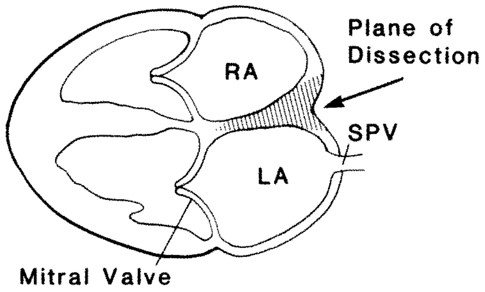


Fig 1. Exposure of the interatrial groove between the sulcus terminalis and the right pulmonary veins depends on developing the proper plane of dissection. (LA = left atrium; RA = right atrium; SPV = superior pulmonary vein.)

Accepted for publication April 13, 1992.

Address reprint requests to Dr Cohn, Division of Cardiac Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

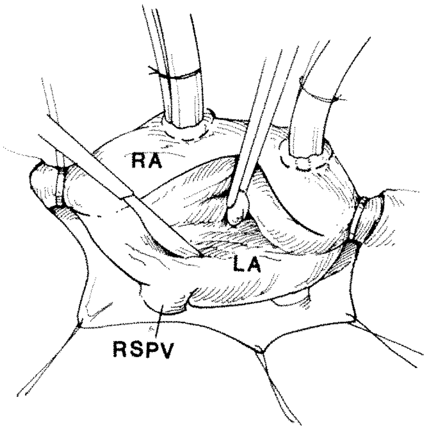


*Fig 2. Development of this plane is achieved by a combination of sharp and blunt dissection reflecting the right atrium (*RA*) anteriorly. (*LA *= left atrium;* RSPV *= right superior pulmonary vein.)*

Fig 4. Operative photograph with right atrium reflected anteriorly by retractors showing the large area of the dome of the left atrium exposed (patient's head to the left, feet to the right).

rightward rotation of the heart [15]. Tilting the operating table head up and rolled away from the surgeon also aids exposure. Stable retraction of the atrial walls is achieved using the Cosgrove self-retaining retractor [1, 6, 7, 15] (Fig 6). A left atrial vent is used to aspirate blood from the dependent portion of the left atrium.

Closure of the incision at the completion of the left atrial procedure is accomplished by a single layer of 3-0 Prolene (Ethicon, Somerville, NJ) in a running suture. Care must be taken to approximate the endocardial surfaces and to exclude any of the fat from the interatrial groove from the suture line. We have not encountered any difficulties with this closure even in very elderly patients or others with fragile atrial tissues. There is no foreshortening of the incision or of the left atrium.

Results

We have used this incision in 348 patients undergoing mitral valve procedures (Table 1) without the need to resort to other maneuvers to visualize the mitral valve. There has been no complication from this incision including bleeding from the suture line in the entire series.

Comment

In the late 1950s and early 1960s, the first mitral valve procedures were reported [16–18] and the valve was approached through a left or right thoracotomy. Dubost and associates [19] first reported the transatrial approach in 1966. Later the incision in the lateral wall of the left atrium, starting in the right superior pulmonary vein, became accepted as the routine approach. Recent interest in mitral reconstructive procedures and reoperations has been associated with a proliferation of publications describing more radical approaches to obtain adequate mitral exposure. These more radical recommendations include the following:

1. Temporary division of the superior vena cava [1, 6, 7]: We have found this unnecessary as simple dissection of the cavae allows adequate mobilization of the heart. The division of the superior vena cava lengthens and complicates the operation as well as risking superior vena caval stenosis and sinoatrial node injury.
2. Transseptal incisions with or without superior extension into the transverse sinus [4, 5, 19–21]: These incisions are complicated and often difficult to close. Extending the incision superiorly into the dome of the

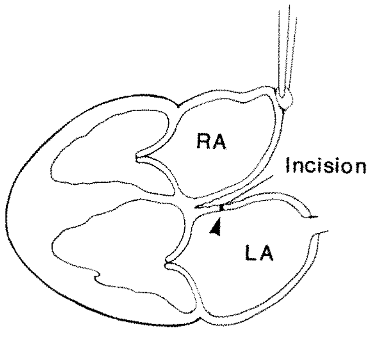


*Fig 3. The most medial and anterior aspect of the left atrium (*LA*) is exposed just adjacent to the interatrial septum. (*RA *= right atrium.)*

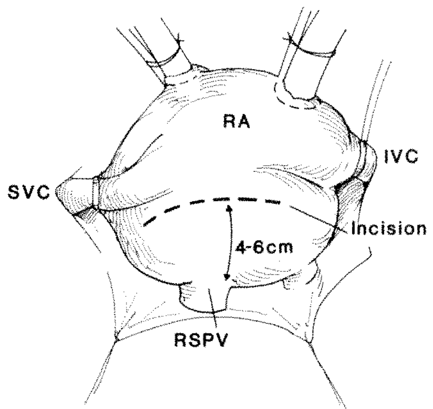


*Fig 5. Incision into the left atrium is then made parallel to the right pulmonary veins 4 to 6 cm closer to the mitral valve. (*IVC *= inferior vena cava;* RA *= right atrium;* RSPV *= right superior pulmonary vein;* SVC *= superior vena cava.)*

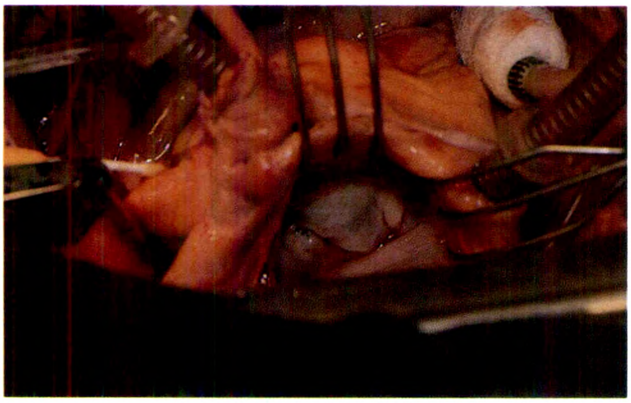


Fig 6. Exposure of the repaired mitral valve bulging from left ventricular fluid. Stable retraction is provided by the arms of the Cosgrove retractor.

atrium risks trauma to the sinus node artery and the potential for either early or late "sick sinus syndrome." Those incisions that employ a transverse septal incision risk tearing of the incision medially with resultant damage of the conducting tissues and heart block.

3. The superior approach [3, 22]: The atrium is entered through its dome in the transverse sinus. This often allows good exposure, however is inadequate in the small left atrium and is not good for electrophysiological procedures, nor repairs of the mitral valve. This incision risks trauma to the sinus node artery as it traverses the atrial dome with the risk of early and late arrhythmias. Aggressive traction of the ascending aorta in the elderly with atherosclerotic aortas can be associated with serious atheroembolization.

The technique using the development of the interatrial groove provides excellent exposure for all left atrial procedures in any sized left atrium. It is a simple dissection that is easy to close. It avoids the risks of trauma to the vital conducting tissues and does not necessarily lengthen or complicate the mitral procedure.

Although this approach is not new, we believe it appropriate to reemphasize this technique at a time when mitral surgery is undergoing a renaissance of interest especially in reconstructive procedures that require excellent stable exposure.

Table 1. Mitral Valve Surgery, 1989–1992 (n = 348)

Operation	Primary	Reop
Mitral valve replacement	145	75
Mitral valve repair	116	7
Mitral valve perivalvar leak	. . .	5
Total	261	87

References

1. Zacharias A. Alternative method to improve exposure for difficult mitral valve procedures. Ann Thorac Surg 1986;42: 336–7.
2. Hirt SW, Frimpong-Boateng K, Borst HG. The superior approach to the mitral valve—is it worthwhile? Eur J Cardiothorac Surg 1988;2:372–6.
3. Kreitmann P, Jourdan J, Saab M, Teboul J, Acar C, Dor V. Abord de la valve mitrale par voie trans-atriale. Intérêt particulier dans les remplacements valvulaires itératifs. Ann Chir 1986;40:557–9.
4. Brawley RK. Improved exposure of the mitral valve in patients with a small left atrium. Ann Thorac Surg 1980;29: 179.
5. Pezzella AT, Effler DB, Levy IE. Operative approaches to the left atrium and mitral valve apparatus. Tex Heart Inst J 1983;10:119–23.
6. Barner HB. Combined superior and right lateral atriotomy with division of the superior vena cava for exposure of the mitral valve. Ann Thorac Surg 1985;40:365–7.
7. Selle JG. Temporary division of the superior vena cava for exceptional mitral valve exposure. J Thorac Cardiovasc Surg 1984;88:302–6.
8. Kyger ER, Coselli M, Kalchoff WP. A method for improved exposure of the mitral valve: cannulation of the innominate vein and division of the superior vena cava for extended left atriotomy in mitral valve operations. J Thorac Cardiovasc Surg 1986;91:143–6.
9. Sondergaard T, Gotzsche M, Ottosen P, Schultz J. Surgical closure of interatrial septal defects by circumclusion. Acta Chir Scand 1955;109:188–96.
10. Cohn LH, Peigh PS, Sell J, DiSesa VJ. Right thoracotomy, femoral bypass, and deep hypothermia for replacement of the mitral valve. Ann Thorac Surg 1988;36:665–76.
11. Jones RE, FitzGerald D, Cohn LH. Reoperative cardiac surgery using a new femoral venous right atrial cannula. J Cardiac Surg 1990;5:170–3.
12. McAlpine WA. Heart and coronary arteries: an anatomical atlas for clinical diagnosis, radiological investigation, and surgical treatment. New York: Springer Verlag, 1975:64.
13. Sabiston DC, Spencer FC. Surgery of the chest. Philadelphia: Saunders, 1990:1395–7.
14. Wilcox BR, Anderson RH. Surgical anatomy of the heart. New York: Gower Medical, 1985.
15. Cosgrove DM. Mitral valve reconstruction. Semin Thorac Cardiovasc Surg 1989;1(2):184–5.
16. Effler DB, Groves LK, Martinez WV, Kolff WJ. Open heart surgery for mitral insufficiency. J Thorac Surg 1958;36:665–76, 690–6.
17. Braunwald NS, Cooper TC, Morrow AG. Complete replacement of the mitral valve. J Thorac Cardiovasc Surg 1960;40: 1–11.
18. Clowes GHA Jr, Traks E, Lim K, Barensky J, Del Quarcio A. Results of open surgical correction of mitral valvular insufficiency and description of technique for approach from the left side. Surgery 1962;51:138–54.
19. Dubost C, Guilmet D, Parades B, et al. Nouvelle technique d'ouverture de l'oreillette gauche en chirurgie a coeur ouvert: l'abord biauriculaire transseptal. Presse Med 1966;74:1607.
20. Campanella C, Cameron E, Feilberg VL. Mitral prosthetic replacement in small left atria. Ann Thorac Surg 1990;50: 836–7.
21. Berreklouw E, Ercan H, Schönberger JP. Combined superior-transseptal approach to the left atrium. Ann Thorac Surg 1991;51:293–5.
22. Saksena DS, Tucker BL, Lindesmith GG, et al. The superior approach to the mitral valve. Ann Thorac Surg 1971;12: 146–53.

Pulmonary "Twinning" Procedure: Use of Lungs From One Donor for Single-Lung Transplantation in Two Recipients

David A. Haydock, MD, Donald E. Low, MD, Elbert P. Trulock, MD,
Larry R. Kaiser, MD, Michael K. Pasque, MD, Ernesto Molmenti, MD, and
Joel D. Cooper, MD

Division of Cardiothoracic Surgery, Washington University School of Medicine, St. Louis, Missouri

Since the introduction of lung transplantation as an option for patients with end-stage respiratory disease in the early 1980s, there have been substantial advances made in the technical aspects of transplantation as well as the early clinical results. With an ever-increasing number of patients being designated suitable candidates for transplantation, the volume of transplants in the foreseeable future will be limited more on the basis of donor lung supply than any other single factor. Pulmonary "twinning" provides an important step in ensuring that all suitable and available donor lungs are utilized whenever feasible. This report reviews the results of 20 single-lung transplantations carried out in five separate transplantation centers using organs retrieved from ten donors. The overall mortality rate in this group of patients was 5%, which compares very favorably with historical controls. No serious problem was noted with respect to increased perioperative morbidity or increased ischemic times in this group of patients. We suggest that this process should be considered and, wherever possible, adopted by all major lung transplant centers.

(Ann Thorac Surg 1992;54:1189–92)

The single greatest restriction to increasing the number of lung transplants remains the limited availability of donor lungs. This is in part due to the fact that lungs are more difficult to obtain than other organs due to their susceptibility to infection and edema after brain death.

One strategy for increasing the number of suitable donor lungs is to employ each of a donor's lungs for separate recipients. Until recently, however, this approach had not been used, primarily because of logistical reasons. As indications for single-lung transplantation have been extended to include recipients with chronic obstructive pulmonary disease, primary pulmonary hypertension, and Eisenmenger's syndrome, there are ever-increasing opportunities to use the second lung for simultaneous transplantation into a different recipient, either in the same institution or in a separate transplant center. We initiated application of this strategy in August 1989, a procedure we refer to as "twinning." This report outlines our experience to date with retrieval, distribution, and transplantation of two lungs from one donor, and includes instances in which both lungs were used at Washington University Medical Center, as well as instances in which we received a lung from another institution which used the opposite lung for one of their recipients.

Lung Retrieval Technique

Acceptable lung donors must have a chest roentgenogram that is entirely clear, an arterial oxygen tension exceeding 300 mm Hg with an inspired oxygen fraction of 1.0 and 5 cm H_2O of positive end-expiratory pressure, and an absence of gross purulent secretions or evidence of aspiration on bronchoscopic examination. In addition, the lungs on gross inspection must have no evidence of serious intrapulmonary pathology, contusion, or previous severe inflammatory disease.

Our technique of lung retrieval has previously been described [1]. Currently, most donor lungs are extracted in conjunction with multiple organ removal for transplantation. We use the same extraction technique, whether we plan to use each lung for separate recipients or are planning a bilateral lung transplantation. The heart is removed before the lungs, leaving a cuff of left atrium containing the four pulmonary veins in situ. To facilitate this, dissection of the intraatrial groove is performed before cardiac extraction to increase the distance between the right pulmonary veins and the interatrial septum, allowing adequate left atrial cuff for both the heart and lung specimens.

Immediately before inflow occlusion of the vena cava, 500 μg of prostaglandin E_1 is injected as a bolus into the pulmonary artery. After venous occlusion and aortic cross-clamping, and at the same time as cardioplegia, the lungs are flushed with 3 L of cold, modified Euro-Collins solution through a large-bore catheter placed in the common pulmonary artery. The cardioplegia is vented from the cardiac end of the divided inferior vena cava, and the

---

Accepted for publication April 14, 1992.

Address reprint requests to Dr Cooper, Division of Cardiothoracic Surgery, Washington University School of Medicine, Suite 3108, Queeny Tower, Barnes Hospital, St. Louis, MO 63110.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

pulmonary flush is vented by excision of the tip of the left atrial appendage. The superior vena cava, aorta, and pulmonary artery are then divided in the usual fashion. Division of the left atrium is accomplished, leaving an adequate cuff on the heart as well as surrounding the four pulmonary veins.

After removal of the heart, the trachea is doubly stapled at its midpoint, and the esophagus is divided between staple lines at the same level as the trachea and at a second point just above the diaphragmatic hiatus. This simplified "en bloc" technique facilitates the ease and efficiency with which the remaining thoracic organs can be removed, thereby avoiding unnecessary delay for the teams responsible for removing the abdominal organs. The lungs are then removed en bloc along with the thoracic aorta and the esophagus.

When the decision is made to separate the lungs for delivery to two separate institutions, the lungs should first be cooled topically by immersion for 10 minutes while a back table is prepared for the dissection. The esophagus is dissected free and discarded. The aorta is similarly trimmed away, taking special care to stay close to the adventitia, especially in the region of the ligamentum arteriosum. We make no attempt to preserve bronchial arteries for revascularization. The pericardium is split up to the level of the common atrial cuff, the cuff is divided vertically midway between the right and left veins, and the pulmonary artery is divided at its bifurcation. After the posterior pericardium is completely divided, dissection is carried up to the carina and the proximal left main bronchus is divided between staple lines just at the tracheal carina. Dissection of the peribronchial tissue should be kept to an absolute minimum in an effort to prevent unnecessary devascularization of the main bronchi. The separated lungs are then placed in appropriate containers for shipment to the recipient hospital. If both lungs are to be used for two separate recipients at the same institution, then it is more convenient to transport the organs to the transplant center before separation.

At the time of transplantation, the left main bronchus is shortened to within one to two cartilaginous rings of the left upper lobe takeoff. On the right, the remainder of the trachea, carina, and one or two cartilaginous rings are excised such that the right main bronchus has been transected one to two rings above the right upper lobe orifice.

Results

Between August 1989 and October 1990, 20 patients, 5 men and 15 women with a mean age of 47.8 years (range, 26 to 63 years), at six separate institutions received single-lung transplants from ten donors. On four occasions, the organs were both used at Washington University Medical Center, and on the other six occasions, the organs were separated at the retrieval institution, with one lung being sent to our transplant center. Table 1 shows the chronology of the twinning procedures as well as the diagnoses of the various recipients.

Table 1. Pulmonary Twinning Procedures[a]

Donor	Date of Transplantation	Recipient 1 (left lung)	Recipient 2 (right lung)
1	08/07/89	Retransplant	Emphysema
2	09/15/89	α_1-Emphysema	Emphysema
3	11/21/89	α_1-Emphysema	PPH
4	12/15/89	Emphysema	PPH
5	02/24/90	*IPF*	EG
6	04/16/90	*Emphysema*	Emphysema
7	04/17/90	Emphysema	EG
8	05/06/90	PPH	*ASD "Eisenmenger's"*
9	07/23/90	Emphysema	*Scleroderma*
10	10/25/90	IPF	*Emphysema*

[a] Recipients at institutions other than the Washington University Transplant Program are indicated in italics.

ASD = atrial septal defect; EG = eosinophilic granuloma; IPF = idiopathic pulmonary fibrosis; PPH = primary pulmonary hypertension.

There were no complications associated with the separation of the two lungs. All airways, arteries, and veins were suitable for anastomosis. There were no documented airway healing complications. One of the 20 recipients died in the hospital 62 days after transplantation of cytomegalovirus (CMV) pneumonitis and hepatorenal failure. There were no other documented early or late deaths, with mean follow-up of 10.8 months (range, 3 to 18 months).

With the exclusion of the 1 patient who died, no patients required prolonged intubation or showed evidence of persistent donor lung dysfunction. The average stay in the intensive care unit was 4.4 days (range, 1 to 20 days), and the average time to discharge from the hospital was 25.1 days (range, 15 to 42 days). Although the donors weighed significantly ($p < 0.05$) more than the recipients (mean difference, 14.5 kg), there were no apparent problems with donor/recipient size mismatch.

The mean ischemic time for the 20 recipients was 4 hours 20 minutes. The site of the transplant and the ischemic times are shown in Table 2. Use of each lung, whether at the same or separate transplant centers, did not adversely affect overall ischemic time.

The assessment of transplantation success very much depends on the original condition being treated. For patients with obstructive disease, we have found assessment of forced expiratory volume in 1 second, room air arterial oxygen tension, and distance walked in 6 minutes to be good indicators of success. With patients with pulmonary hypertension, improvement in pulmonary artery pressures and right ventricular ejection fractions are the more important parameters. Consequently, the results of the 14 patients who received their transplant at Washington University Medical Center are divided into two sections.

Obstructive Lung Disease

Room air arterial oxygen tension was seen to improve significantly ($p < 0.05$) from 54.5 ± 11.5 mm Hg at initial pretransplantation evaluation to 71.0 ± 8.9 mm Hg just

Table 2. Lung Retrievals in Twinning Procedures

		Left Lung		Right Lung	
Donor	Retrieval Site	Transplantation Site	Ischemic Time (min)	Transplantation Site	Ischemic Time (min)
1	Miami	WUMC	279	WUMC	350
2	St. Petersburg	WUMC	265	WUMC	302
3	Minneapolis	Univ. of Minnesota	212	WUMC	290
4	Jacksonville	WUMC	321	WUMC	340
5	Toronto	Univ. of Toronto	93	WUMC	330
6	Winston/Salem	N. Carolina Baptist Hospital	166	WUMC	315
7	Chapel Hill	WUMC	266	Univ. of N. Carolina	223
8	Kansas City	WUMC	290	WUMC	270
9	Oklahoma City	WUMC	270	Univ. of Texas	137
10	Toronto	WUMC	332	Univ. of Toronto	120

WUMC = Washington University Medical Center.

before discharge. In addition, all patients were requiring at least intermittent oxygen therapy before transplantation and no patient required oxygen therapy at the time of discharge.

Forced expiratory volume in 1 second values compared at the time of pretransplantation evaluation and 1 month after transplantation were seen to significantly improve ($p < 0.05$). The mean forced expiratory volume in 1 second at evaluation was 519 ± 146 mL. One month after transplantation, the mean level had increased to 1,295 ± 190 mL. At the time of initial assessment, all patients with chronic obstructive pulmonary disease required supplemental oxygen therapy (mean, 5.5 L/min; range, 2 to 12 L/min) to complete the 6-minute walk. However, no patients required oxygen after transplant to complete the examination. The mean distance walked in 6 minutes before transplantation was 232 ± 108 m. At 3 months after transplantation, mean distance walked had significantly improved to 567 ± 121 m ($p < 0.05$).

Pulmonary Hypertension and Restrictive Lung Disease

The 4 patients with pulmonary hypertension have all demonstrated a significant improvement as reflected in a decrease in pulmonary artery pressure and an increase in right heart ejection fraction. Pulmonary artery pressure was seen to decrease from 57.5 ± 2.9 mm Hg before transplantation to 17.5 ± 9.0 mm Hg at 3 months after transplantation. Right ventricular ejection fraction, as measured by radionucleotide ventriculogram, was seen to improve from 0.29 ± 0.11 before transplantation to 0.52 ± 0.21 after transplantation.

The single patient who underwent transplantation for restrictive lung disease demonstrated improvement in spirometry, room air arterial oxygen tension levels, and distance walked in 6 minutes when levels from before transplantation and 4 to 6 weeks after transplantation were compared. Forced vital capacity went from 1.88 L (53% predicted) to 2.38 L (67% predicted), and total lung capacity improved from 2.47 L (43% predicted) to 3.33 L (58% predicted). Room air arterial oxygen tension went from 46.7 mm Hg to 70.6 mm Hg, and 6-minute walk distance increased from 197 to 480 m.

Complications

Of the 14 patients in our institution for whom we have detailed information, supraventricular tachycardia (atrial fibrillation/flutter) occurred in 4, wound infection in 1, and a cervical herniated disc in 1. Although no "twins" had development of pneumonia due to the same organism, clinical evidence of bacterial chest infection developed in 3 patients. However, on no occasion had the responsible organism been previously cultured from the donor bronchial washing. Two other patients had persistent left lower lobe collapse that resolved before discharge.

Of the 4 patients from the Washington University Transplant Program who were found to be serologically negative for CMV but had received lungs from CMV-positive donors, 3 were found to have evidence of CMV pneumonitis demonstrated on bronchoscopy and transbronchial biopsy. Of the 8 patients who were found to be CMV-positive before transplantation, 4 were found to have evidence of CMV pneumonitis. In neither of the 2 patients who were originally CMV-negative and received lungs from CMV-negative donors did any evidence of CMV develop.

Comment

Owing to the difficulty of obtaining suitable donor lungs, and the large number of recipients currently waiting for pulmonary transplantation, efforts have been made to maximally utilize all appropriate donor lungs that become available. In general efforts that have been shown to be effective include increased publicity to encourage organ donation and increased physician awareness when dealing with potential donors and their families [2]. These efforts currently include increased attention to donor management before organ retrieval, increased flexibility with respect to the matching of donor dimensions (especially in patients with emphysema), and using single instead of bilateral lung replacement whenever it seems justifiable.

This report demonstrates that twinning or donor lung sharing procedures can be performed with satisfactory results and without an increase in major complications arising from such sharing. It also demonstrates the feasibility of simultaneous single-lung transplantations in a single institution. Our first "twins" (see Table 1) included a patient undergoing repeat transplantation due to primary organ failure 12 days after his initial left lung replacement. The fourth "twins" were 2 patients with pulmonary hypertension (one primary and one secondary to a large atrial septal defect).

Undoubtedly the easiest pairing occurs when both patients have emphysema. These operations tend to be technically straightforward compared with operations on patients with restrictive disease or pulmonary hypertension. In addition, cardiopulmonary bypass is very rarely required when transplanting for emphysema, whereas it has been routinely used in transplantations for pulmonary hypertension.

The ability to accommodate a simultaneous twinning procedure in one institution requires adequate staff and facilities as well as a sizable pool of waiting recipients. All patients undergo preoperative, quantitative lung ventilation/perfusion scans. In patients with ventilation and perfusion mismatches favoring one side, choosing the side with the poorest function for lung replacement will increase the chances of avoiding the need for cardiopulmonary bypass and simplify the logistics. Those patients with suitable pulmonary pathology and whose lung function is evenly shared between sides often serve as the best candidates for the twinning procedure, as they can accept either a left or a right lung, depending on which is available.

The ability to mount two full transplant teams familiar with all aspects of lung transplantation, and to have available a third team for retrieval purposes, will likely be the limiting factor at many institutions. The primary benefit of the twinning procedure is the sharing of the two lungs between transplant centers. This can be accomplished even when the two institutions are a considerable distance from each other.

As more centers become experienced with lung retrieval, the potential for lung sharing will correspondingly increase. The longest ischemic time experienced in the 20 patients in this report was 5 hours 50 minutes, well within the current limits of safety. Anticipated improvements in lung preservation will further simplify the logistics of sharing lungs between institutions that are remote from each other.

One incidental byproduct of twinning procedures is the biologic experiment inherent with the process. Both lungs are genetically identical and undergo a completely similar preservation process. As a result, subsequent events, including technical and recipient factors, must be the determinants when assessing outcome with the separate grafts. As the number of these procedures being performed in patients with identical diagnoses increases, it will be possible to make comparisons with respect to the influence of individual recipient factors and technical differences on the ultimate result. Of particular interest will be the frequency and severity of bacterial and viral infections that occur in the recipients and the relationship, if any, to donor factors.

In conclusion, this experience demonstrates that twinning provides a valuable method for maximally utilizing all available donor lung grafts for transplantation into separate recipients. With little additional organization, single-lung transplantations can be carried out in two separate institutions after the harvest of a double-lung block from a single donor. In addition, the results demonstrate the potential for successful simultaneous single-lung transplantation in one institution. These procedures can be done with short-term and long-term results comparable with those seen in previous series of single-lung transplantations, where twinning procedures were not used.

We would like to acknowledge the participation and cooperation of those programs with whom we shared lungs and retrievals: The University of Toronto, The University of Minnesota, The University of North Carolina at Chapel Hill, and The University of Texas at San Antonio.

We would also like to acknowledge Mid American Transplant, whose ability to respond quickly enabled sharing to occur on short notice, and with minimum delay.

References

1. Todd TR, Goldberg M, Koshal A, et al. Separate extraction of cardiac and pulmonary grafts from a single organ donor. Ann Thorac Surg 1988;46:356–9.
2. Gore SM, Taylor RMR, Wallwork J. Availability of transplantable organs from brain stem dead donors in intensive care units. Br Med J 1991;302:149–53.

Radical Laser Segmentectomy for T1 N0 Lung Cancer

Ken Kodama, MD, Osamu Doi, MD, Takushi Yasuda, MD, Masahiko Higashiyama, MD, and Hideoki Yokouchi, MD

Department of Thoracic Surgery, The Center for Adult Diseases, Osaka, Japan

Over the last 40 months, 18 lung cancer patients with T1 N0 non–small cell lung carcinoma have been treated with radical laser segmentectomy. This innovative operative method consists of a combination of anatomical or nonanatomical segmentectomy by neodymium:yttrium-aluminum garnet laser parenchyma sparing with complete hilar lymph node dissection. Although the median follow-up period is too short, there is no local recurrence and no cancer deaths. There have been no major complications. Even deep-seated tumors can be resected with a clear safety margin using this method. Radical laser segmentectomy may be a useful adjunct to preserve normal lung tissue and to perform very radical resection.

(Ann Thorac Surg 1992;54:1193–5)

For a long time, lobectomy has been widely accepted as a standard technique in the surgical treatment of primary lung cancer. However, this approach requires the removal of more than one-fifth of the total lung volume (with the exception of middle lobe resection). Removing such a large normal portion of the lung leads to loss of lung function.

Recently, exact preoperative and intraoperative evaluation of the tumor extension has become possible by using computed tomographic scanning and intraoperative histodiagnosis of frozen sections. Also, conservative resection for lung cancer with the objective of preserving lung function in patients with T1 N0 lesions has been carried out with good survival rates [1].

We have developed an innovative technique that combines segmentectomy using a neodymium:yttrium-aluminum garnet (Nd:YAG) laser and hilar lymph node dissection. This approach enables us to preserve lung function and perform radical resection in the case of T1 N0 lung cancers originating on the peripheral lung parenchyma or a bronchus distal from a segmental bronchus.

Clinical Summary

Over the last 40 months, 4 women and 14 men between the ages of 46 and 81 years (mean age, 64 years) with non–small cell lung carcinoma have been treated with laser segmentectomy. Informed consent was obtained from candidates for pulmonary resection. Patients eligible for this procedure were those who had peripheral small lesions of less than 3 cm in diameter (n = 16) or had small endobronchial lesions located distal from the segmental bronchus (n = 2). Evaluation of the clinical stage was performed with a computed tomographic scan. The tumor locations and histologic classifications are listed in Table 1. The most common site of the tumor was in the right posteroapical segment (S6) of the lower lobe.

Operative Technique

A lateral thoracotomy with muscle sparing in the fourth or fifth intercostal space was performed [2]. First, the interlobular and lobular pulmonary arteries and veins are isolated. The drainage vessels to the pulmonary segment including the tumor are ligated and divided. Then, the regional lymph nodes surrounding these vessels and bronchus are dissected along with connective tissues. Intraoperative histodiagnosis of these dissected specimens is performed by using frozen sections. The segmental bronchus is divided and closed with interrupted 4-0 polypropylene sutures.

After the hilar management, parenchyma sparing of the lung is performed by using an Nd:YAG laser (Fig 1). The laser equipment consists of a MediLas 2 type 621 Nd:YAG laser (MBB-Medical Technology Ltd, Munich, Germany). Precise details of how to use this laser have been described by us previously [3]. While the lung is inflated, anatomical or nonanatomical resection of the parenchyma is carried out with the noncontact laser focusing handpiece; a constant safety margin of about 3 cm from the tumor edge is maintained (see Fig 1A). The small vessels and bronchioles that appear on the laser-irradiated field must be carefully ligated. Furthermore, they are overlaid with fibrin glue. An illustration of the operation after completion is presented in Figure 2. The total laser power required for this procedure ranged from 7,933 to 34,145 J (average, 17,148 J).

The 2 patients who had small endobronchial lesions

Accepted for publication April 17, 1992.

Address reprint requests to Dr Kodama, Department of Thoracic Surgery, The Center for Adult Diseases, 3 Nakamichi 1-chome, Higashinari-ku, Osaka 537, Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Summary of Patient Data

Variable	No. of Patients
Histology	
Adenocarcinoma	11
Squamous cell	5
Large cell	2
Tumor diameter	
<1 cm	2
1–2 cm	4
2–3 cm	12
Segment resected	
Right	
S6	6
S2	3
S3	1
Left	
S4 + 5	2
S6	2
S1 + 2 + 3	1
S1 + 2 + 4	1
S1 + 2	1
S4	1

distal from the segmental bronchus required an additional bronchoplastic procedure.

Comment

The Nd:YAG laser has proved to be an useful tool in the local excision of nodular lesions such as benign pulmonary tumors or metastatic lesions from other sites [3–5]. Recently, Landreneau and co-workers [6] reported that the laser can be useful for limited pulmonary resection, emphasizing that careful attention to the segmental bronchopulmonary anatomy is essential during the dissection to avoid injury to the surrounding lung parenchyma.

In a randomized trial conducted by the North American Lung Cancer Study Group [7] comparing limited resection (wedge and segmental resection) to lobectomy for T1 N0 non–small cell lung cancer, there was a statistically significant increase in the local recurrence rate (2.7-fold). On the other hand, Read and co-workers [1] reported that segmentectomy can be used with minimal risk of local recurrence. However, tumor characteristics such as size, histology, and bronchial invasion should be considered when selecting operation methods [1]. The approach we have developed for T1 N0 disease includes hilar lymph node dissection and laser-assisted parenchyma sparing. In addition, sampling of the lymph nodes in the mediastinum is performed. We have named this new approach "radical laser segmentectomy."

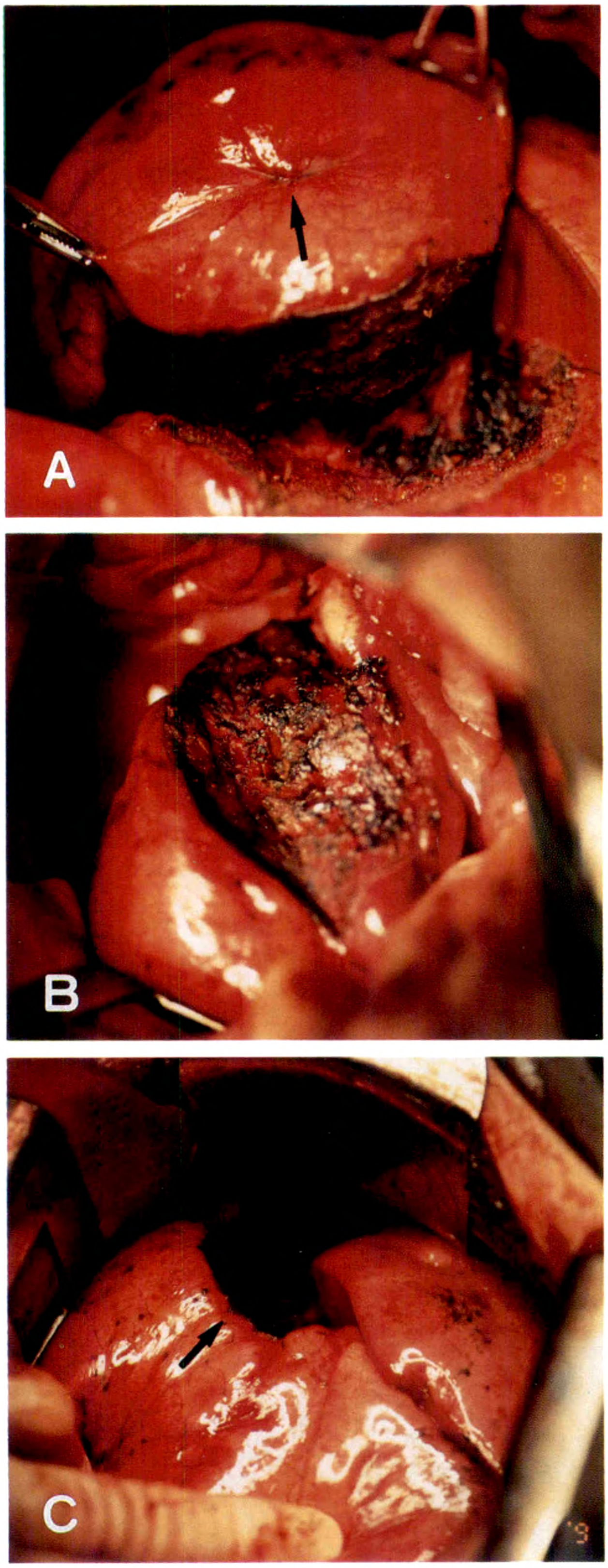


Fig 1. Intraoperative photographs of right S6 radical laser segmentectomy (A) Nonanatomical laser sparing of the lung parenchyma was carried out with a constant margin around a tumor located just under the slightly umbilicated visceral pleura (arrow). *(B) Bronchioles and vessels appearing on the spared surface were carefully ligated and overlaid with fibrin glue. (C) When the residual lung was inflated, the pleural space problem was minimized* (arrow).

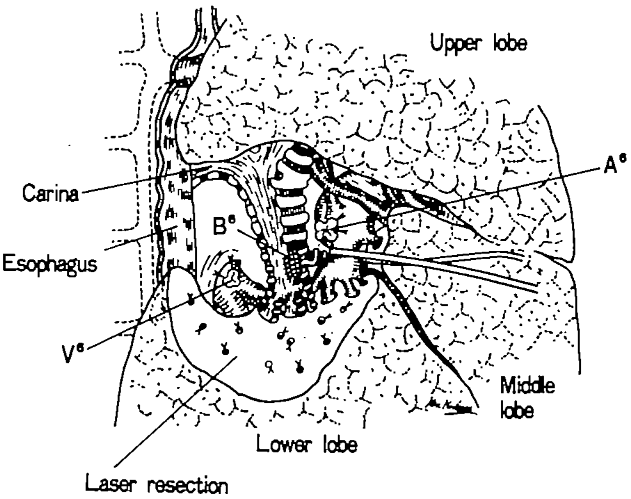


Fig 2. The operative scheme after completion of radical laser segmentectomy. Interlobar and lower lobe lymph nodes are completely dissected.

Complications experienced in our series consisted of 1 case of bronchiolar fistula and 1 case of bronchial fistula. The former patient was successfully treated with chest tube drainage. In the latter patient, there was no direct relationship between the bronchial fistula and laser treatment, because the laser was not irradiated to the bronchial stump. However, this patient had severe diabetes mellitus. In this patient, to close the fistula, it was necessary to operate again, ie, omentopexy was performed.

As a result of laser irradiation, small vessels and bronchioles with a diameter of a few millimeters readily become detached from the lung parenchyma and are exposed. To prevent small air leaks such as occurred in our first patient with complications, it is important to carefully ligate such detached vessels and bronchioles (see Fig 2). Recently, we have begun treating the laser-irradiated field not just with fibrin glue, but also with collagen powder, which is applied in several layers. This technique is achieving good results in preventing air leakage. In addition, for patients such as our second patient with complications, who are at risk of requiring a long time for wound healing, we have recently begun trying a technique in which the bronchial stump is covered with a pedicle flap created from substernal fat pad.

If intraoperative histodiagnosis reveals lymph node metastases or malignant cells in the bronchial stump, we must then change the operative procedure from segmentectomy to standard lobectomy with mediastinal lymph node dissection. We have experienced only 2 cases in which this change of procedure was necessary; they are not included in this study.

If needed, we recommend that nonanatomical segmentectomy be performed to obtain a safety margin that is sufficient to prevent local recurrence. The function of residual neighboring segments can be preserved in two ways: ventilation through a "pore of Korn," and circulatory connection with other intact segmental vessels.

Attempting stapled resection of the lung parenchyma could result in substantial pulmonary distortion leading to impairment of the local circulation, loss of function of the surrounding lung tissue, and possible pleural space problems [6]. In addition, it is difficult to keep a safety margin that is equally distant from the tumor edge. With our technique, distortion of the residual lung is not found (see Fig 1B) and the pleural space problem is minimized (see Fig 1C). By using the laser for parenchyma sparing, a sufficient safety margin can be obtained not only for superficial tumors, but also for deep-seated tumors.

Our findings to date suggest that radical laser segmentectomy is a safe and effective approach for use in patients with T1 N0 lung cancer, providing both a radical operation and functional preservation. Careful long-term follow-up is essential, and a prospective, randomized study for comparison of local recurrence between our method and lobectomy is planned in the near future.

References

1. Read RC, Yoder G, Schaeffer RC. Survival after conservative resection for T1 N0 M0 non–small cell lung cancer. Ann Thorac Surg 1990;49:391–400.
2. Hazelrigg SR, Landreneau RJ, Boley TM, et al. The effect of muscle-sparing versus standard posterolateral thoracotomy on pulmonary function, muscle strength, and postoperative pain. J Thorac Cardiovasc Surg 1991;101:394–401.
3. Kodama K, Doi O, Higashiyama M, Tatsuta M, Iwanaga T. Surgical management of lung metastases. Usefulness of resection with the neodymium:yttrium-aluminum-garnet laser with median sternotomy. J Thorac Cardiovasc Surg 1991;101:901–8.
4. Moghissi K. Local excision of pulmonary nodular (coin) lesion with noncontact yttrium:aluminum-garnet laser. J Thorac Cardiovasc Surg 1989;97:147–51.
5. LoCicero J III, Frederiksen JW, Hartz RS, Michaelis LL. Laser-assisted parenchyma-sparing pulmonary resection. J Thorac Cardiovasc Surg 1989;97:732–6.
6. Landreneau RJ, Hazelrigg SR, Johnson JA, Boley TM, Nawarawong W, Curtis JJ. Neodymium:yttrium-aluminum garnet laser–assisted pulmonary resections. Ann Thorac Surg 1991;51:973–8.
7. Ginsberg RJ, Rubinstein L, for the Lung Cancer Study Group. Patients with T1 N0 non–SCLC lung cancer. Lung Cancer 1991;7(Suppl):83.

Quantitation of Particulate Microemboli During Cardiopulmonary Bypass: Experimental and Clinical Studies

Jin-Feng Liu, MD, Zhao-Kang Su, MD, and Wen-Xiang Ding, MD

Department of Pediatric Cardiothoracic Surgery, Xin Hua Hospital, Shanghai Second Medical University, Shanghai, People's Republic of China

An electronic particle-size analyzer (Coulter Counter ZM) was used to quantitate particulate microemboli 15 to 80 μm in size during cardiopulmonary bypass. Through both laboratory studies and clinical research, we confirmed three main causes of microemboli: (1) infusion of banked blood stored for more than 3 days; (2) use of cardiotomy reservoirs; and (3) use of bubble oxygenators. The regression equation between number of particles and blood storage time was $Y = 3.7262X + 10.244$ ($r = 0.886$; $p < 0.01$). The number of microemboli from cardiotomy reservoirs was 2.8 to 5.1 times that from other sources ($p < 0.01$). The number of solid particles from bubble oxygenators was 1.8 to 3.2 times that from membrane oxygenators ($p < 0.01$). Electron microscopy showed that a large number of solid particles more than 20 μm in size were formed during heart-lung bypass. They obstructed the microcirculation and damaged pulmonary capillary endothelial and alveolar epithelial cells. The degree of histological damage was related to the number and size of microemboli and the duration of pulmonary microcirculatory obstruction.

(Ann Thorac Surg 1992;54:1196–202)

Extracorporeal circulation in open heart surgery is associated with many pathophysiological changes resulting in impairment of the brain, heart, lungs, and kidneys [1]. One major complication is microembolism, which causes microcirculatory obstruction [2, 3]. There are two kinds of microemboli, gaseous particles and solid particles. The occurrence of air embolism has been markedly decreased by improvements in operative technique and in filter and oxygenator design, whereas solid particles have become more important as causes of embolism [4].

Methods for the quantitation of microparticles have included microscopic examination of the filter membrane after filtration, measurement of screen filtration pressure, and ultrasound. The first two can be influenced by environmental factors and cannot differentiate cell or platelet adhesion from aggregation. Ultrasound cannot detect particles smaller than 50 μm and is more sensitive to air bubbles than solid particles. The electronic particle counter (Coulter Counter ZM, Coulter Electronics, Luton, Bedfordshire, England), introduced in the 1970s, is very sensitive and accurate in quantitating solid particles [5–9]. The Coulter Counter ZM is a precision dual-threshold particle-counting and sizing instrument for matter in the overall size range of 0.4 to 800 μm.

Using the electronic particle-size analyzer and the Cell-DYN 900 blood analyzer (Sequoia-Turner Corporation, Mountain View, CA), we carried out experiments to investigate the causes of destruction of blood cells and the formation of solid microparticles. We examined the correlation between the number and the size of the particles, their effect on the pulmonary ultrastructure, and methods to prevent and reduce solid microparticles in blood during extracorporeal circulation.

Material and Methods

In Vitro Study

The in vitro study involved a perfusion circuit and acid-citrate-dextrose bovine blood stored for 1 day to 3 days. It comprised four experimental groups: group a, perfusion circuit with a roller pump (Sarns 7400); group b, perfusion circuit with a roller pump and a bubble oxygenator (Shanghai Medical Diagnostic Instrument Factory); group c, perfusion circuit with a roller pump and a membrane oxygenator (Scientific Instrument, FuDan University, Shanghai); and group d, perfusion circuit with a roller pump, a membrane oxygenator, and a cardiotomy suction

Table 1. Clinical Data on the Two Patient Groups

Variable	Bubble Oxygenator (n = 10)	Membrane (n = 10)
Age (y)	6.3 ± 1.6	4.4 ± 1.3
Weight (kg)	19.1 ± 4.9	12.5 ± 2.5
Hematocrit	0.221 ± 0.024	0.218 ± 0.031
Bypass flow ($mL \cdot kg^{-1} \cdot min^{-1}$)	100–500	100–150
Gas/blood ratio	3:1	0.5–1:1
Bypass time (min)	48 ± 7.6	81 ± 26

Accepted for publication July 20, 1992.

Address reprint requests to Dr Liu, Department of Pediatric Cardiothoracic Surgery, Xin Hua Hospital, 1665 Kong Jiang Rd, Shanghai, People's Republic of China 200092.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

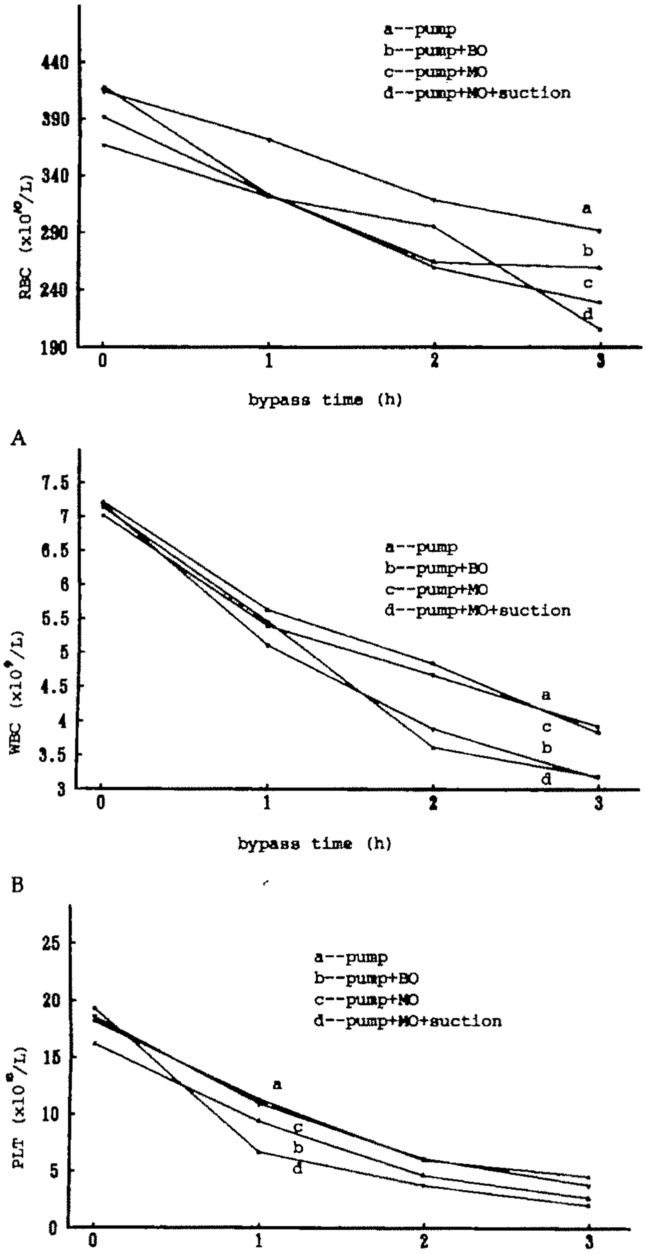


Fig 1. *Destruction of (A) red blood cells (RBC), (B) white blood cells (WBC), and (C) platelets (PLT) relative to duration of perfusion on the circuit in the four in vitro experimental groups (a–d).* (BO = *bubble oxygenator;* MO = *membrane oxygenator.)*

system. The blood prime was heparinized (2 mg/100 mL), and the hematocrit was 0.25 to 0.30. The perfusion rate was 2 L/min for 3 hours. The gas to blood flow ratio was 3:1 for the bubble oxygenator, 0.5–1:1 for the membrane oxygenator, and 1–3:1 for the cardiotomy suction system. Blood samples were taken before the perfusion circuit was started and every hour during perfusion for determination of red blood cell, white blood cell, and platelet counts, plasma-free hemoglobin levels, and microparticle

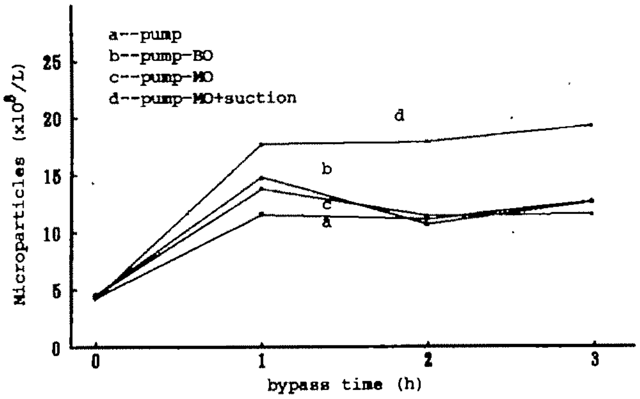


Fig 2. *Number of microparticles 15 to 80 μm in diameter detected in the in vitro circuits used in groups a, b, c, and d.* (BO = *bubble oxygenator;* MO = *membrane oxygenator.)*

count, with particular attention paid to the number and distribution of particles 15 to 80 μm in diameter. The experiment was repeated five times for each group.

Eighty-four bags of acid-citrate-dextrose banked blood were randomly selected for study. The blood was divided into seven groups according to storage time, with 12 bags per group. Red blood cell, white blood cell, platelet, and particle counts were done before and after blood passed the filter.

Animal Study

Twenty dogs weighing 10 to 16 kg (mean weight, 12.6 ± 2.1 kg) were divided into three groups. In group 1 (n = 4), cardiopulmonary bypass (CPB) was undertaken with a membrane oxygenator; this was the control group. In group 2 (n = 8), standard polyvinyl chloride particles 13, 20, 45, and 75 μm in size were injected into the right atrium before bypass. During bypass, rectal temperature was maintained at 28° to 30°C and hematocrit, at 0.20 to 0.25. The perfusion rate was 100 to 150 mL $\cdot$ kg^{-1} $\cdot$ min^{-1}. Cardiopulmonary bypass lasted 3 hours. The gas to blood flow ratio for the oxygenator was 1:1, and the heparin dose was 2 mg/kg. No filter was used in the extracorporeal

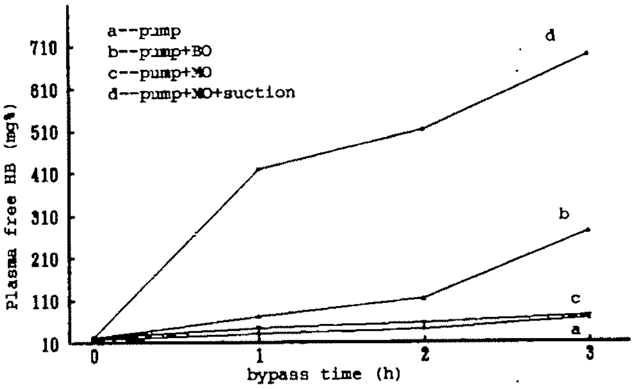


Fig 3. *Increase in plasma free hemoglobin (HB) relative to duration of perfusion on the circuit in the in vitro experimental groups (a–d).* (BO = *bubble oxygenator;* MO = *membrane oxygenator.)*

Table 2. Comparison of Four Variables Between Fresh and Banked Blood

Variable	Fresh Heparinized Blood	Days of Storage of Banked Blood						
		1	3	5	7	10	14	21
RBC ($\times 10^{12}$ L)	3.9 ± 0.2	3.8 ± 0.2	3.4 ± 0.2	3.3 ± 0.3	2.9 ± 0.3	2.8 ± 0.3	2.5 ± 0.5	1.8 ± 0.5
WBC ($\times 10^9$/L)	7.2 ± 1.6	5.1 ± 1.4	4.0 ± 0.8	3.5 ± 0.4	3.1 ± 0.2	2.8 ± 0.2	2.4 ± 0.2	1.9 ± 0.4
Plt ($\times 10^9$/L)	200 ± 30	140 ± 30	70 ± 2.0	30 ± 1.0	<10	<10	<10	<10
Particles ($\times 10^9$/L)	3.9 ± 0.7	7.3 ± 3.7	8.7 ± 1.8	42.4 ± 10.3	51.1 ± 7.4	48.3 ± 8.7	58.7 ± 6.9	94.8 ± 19.8

Plt = platelets; RBC = red blood cells; WBC = white blood cells.

circuit. Blood samples for the measurement of particles 15 to 80 μm in size were collected from the femoral artery and the venous line before bypass and at 30, 60, 90, 120, and 180 minutes after bypass. Biopsy samples from the middle of the right lung were taken before and after bypass for electron microscopic examination. In group 3 (n = 8), standard 13-, 20-, 45-, and 75-μm particles were injected into the right atrium after the chest was opened. Arterial and venous blood samples were taken before and at 30 and 60 minutes after injection for particle measurement and electron microscopic examination.

Clinical Study

Twenty patients with noncyanotic congenital heart diseases who were undergoing an open heart operation were selected for the study. They were divided into two equal groups: a bubble oxygenator group and a membrane oxygenator group (Table 1). In the extracorporeal circuit system, blood collected from the cardiotomy suction reservoir passed through a mesh with 55-μm pores (Shanghai Xin Hua Hospital Pediatric Cardiothoracic Surgery Laboratories). Heparin, 2 mg/kg, was given by intracardiac injection, and 1 to 2 mg/100 mL was added to the prime. The activated clotting time was prolonged to greater than 600 seconds during CPB.

Before bypass, blood samples for particle measurement were taken from the patient's arterial blood and the prime. Blood samples also were obtained from the extracorporeal venous line, the outlet of the oxygenator, the arterial line distal to the pump, and the cardiotomy reservoir 5 minutes and 30 minutes after the beginning of bypass and immediately after the termination of bypass and were examined for the presence of 15- to 80-μm particles and red blood cell, white blood cell, and platelet counts, hematocrit, and plasma free hemoglobin level. Several kinds of filters were compared: (1) blood transfusion filters with a pore size of 40 μm (Shanghai Xin Hua Hospital Pediatric Cardiothoracic Surgery Laboratories), 55 μm (Pall Biomedical Products), and 170 μm (Shanghai Medical Diagnostic Instrument Factory); (2) prime filter, pore size of 5 μm (Shiley Inc); (3) arterial line filter, pore size of 150 μm (Shanghai Xin Hua Hospital Pediatric Cardiothoracic Surgery Laboratories); and (4) cardiotomy reservoir filter, pore size of 55 μm (Shanghai Xin Hua Hospital Pediatric Cardiothoracic Surgery Laboratories). Blood particles were counted before and after filtration. Filter meshes and filter membrane surfaces were examined by light microscopy.

Results

In Vitro Study

The in vitro experiments demonstrated destruction of blood elements by the perfusion circuit. The order of the severity of destruction by different parts of the circuit was as follows: cardiotomy reservoir, bubble oxygenator, membrane oxygenator, and roller pump (Fig 1). There was no significant difference between the last two components of the circuit ($p > 0.05$). The degree of destruction, which was most significant in the first hour, was linearly correlated with the time of perfusion on the circuit. The number of microparticles in the blood was significantly increased ($p < 0.05$) in the first hour on the perfusion circuit in all groups, but there was no significant change thereafter ($p > 0.05$) (Fig 2). The increasing level of plasma free hemoglobin was most closely related to the time on the perfusion circuit, especially in the circuit containing a cardiotomy reservoir (group d) where the degree of increase was three to eight times higher than in the other components ($p < 0.01$) (Fig 3).

The studies showed that stored acid-citrate-dextrose blood contains many 15- to 80-μm particles. The number

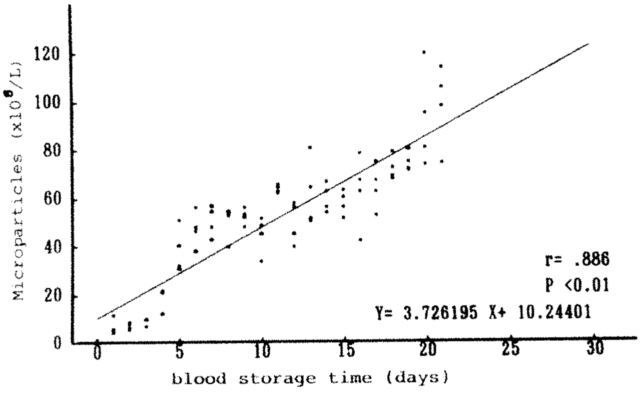


Fig 4. Relationship between blood storage time and number of microparticles 15 to 80 μm in diameter.

Table 3. Changes in Pulmonary Ultrastructure in Animal Experiments[a]

Group[b]	Edema and Rupture of Endothelial Cells	Discontinuity of Collagen and Elastin Fibrils	Lysosomal Granules of Plts and WBCs in Interstitial Tissue	Swelling, Rupture, and Denaturation of Types I, II Epithelial Cells
1 (n = 4)	±	±	–	–
2[c] (n = 8)				
13	+	+	–	–
20	++	+	±	±
45	+++	++	+	+
75	+++	++	++	++
3[c] (n = 8)				
13	±	–	–	–
20	±	–	±	–
45	+	+	±	±
75	+	++	+	+

[a] The degrees of danger were as follows: – = no damage; ± = doubtful damage; + = definite damage; ++ = obvious damage; +++ = severe damage. [b] Group 1 had a membrane oxygenator and served as the control group; group 2, a membrane oxygenator and injection of standardized particles; group 3, injection of standard-sized particles. [c] Minuses indicate the size of the particles injected in micrometers.

Plts = platelets; WBC = white blood cells.

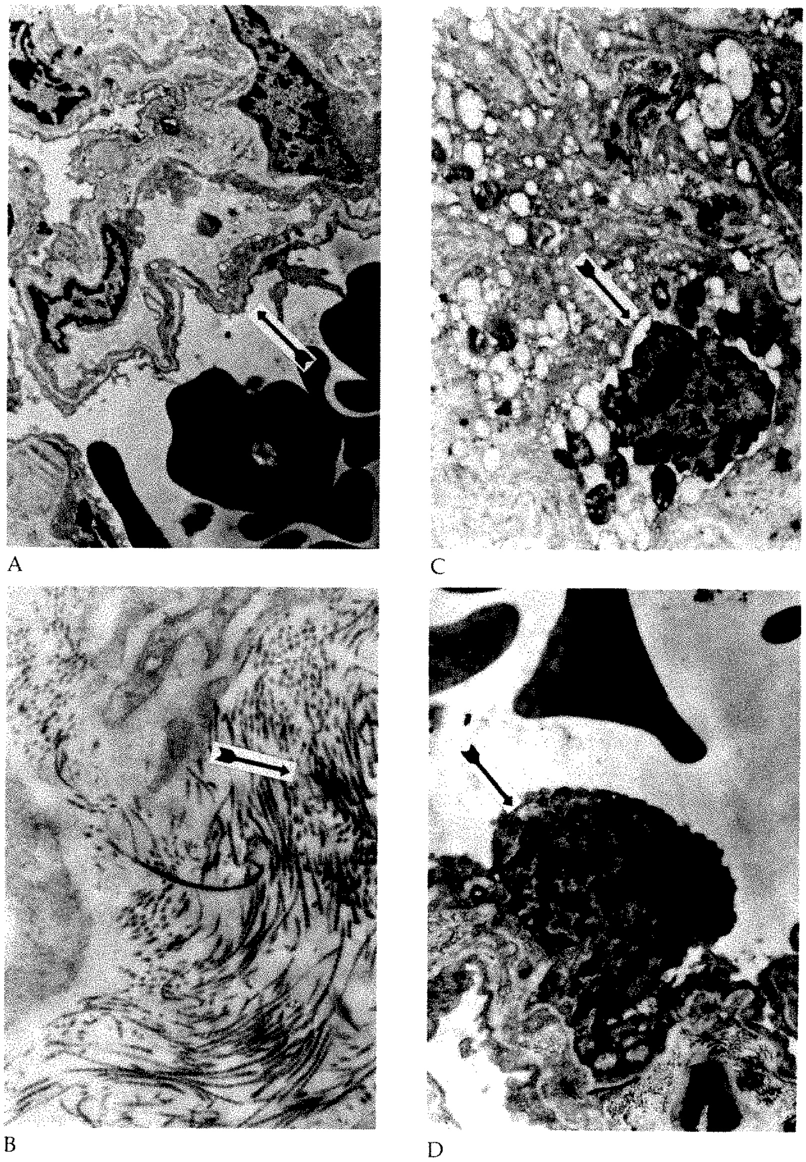


Fig 5. Changes in pulmonary ultrastructure in animal experiments: (A) edema and rupture of endothelial cells (arrow)*; (B) discontinuity of collagen and elastin fibrils* (arrow)*; (C) lysosomal granules of platelets and white blood cells in interstitial tissue* (arrow)*; and (D) swelling, rupture, and denaturation of types I and II epithelial cells* (arrow)*. (A, ×3600; B and C, ×5000; D, ×6000.)*

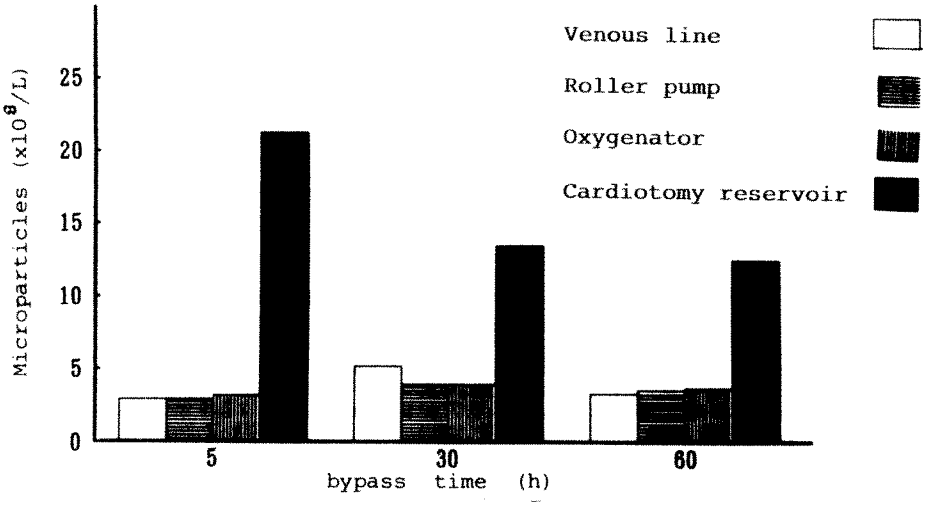


Fig 6. Number of microparticles from different components of the cardiopulmonary bypass circuit.

of particles in blood stored for 5 days was almost 11 times higher than the number in fresh blood (Table 2). The regression equation between particulate number and blood storage time was $Y = 3.7262X + 10.244$ ($r = 0.886$; $p < 0.01$) (Fig 4).

Animal Study

The animal experiments showed that pathological changes in pulmonary ultrastructure after extracorporeal circulation were linearly correlated with the number of microparticles produced during bypass. The size of the microparticles was also important; those greater than 20 μm in size caused damage to the pulmonary ultrastructure. The bigger the particles, the more severe the damage (Table 3; Fig 5).

Clinical Study

These studies demonstrated that the tubing system of the extracorporeal circuit contained many exogenous microparticles. After simple perfusion of the extracorporeal circuit primed with normal saline solution for 10 minutes, the 15- to 80-μm particle count reached 199 ± 69/mL, 14 times higher than before perfusion ($p < 0.001$). The main source of microparticles during extracorporeal circulation was the cardiotomy reservoir, which produced 2.8 to 5.1 times the number from other sources ($p < 0.01$) (Fig 6). Microparticles produced by the bubble oxygenator were 1.8 to 3.2 times more numerous than the number from the membrane oxygenator ($p < 0.01$) (Fig 7). With the prolongation of extracorporeal circulation, the difference became even more significant.

We found that the prime filter (pore size, 5 μm) could remove 87% of the particles in the prime; the cardiotomy reservoir filter (pore size, 55 μm) removed 57% of the particles resulting from suction; and the blood transfusion filter with a pore size of 55 μm removed 59% of the particles in banked blood. Filters with a pore size larger than 150 μm were ineffective in removing microparticles (Fig 8).

Comment

The sources of solid particles in blood during extracorporeal circulation can be classified as intrinsic and extrinsic. After simple bypass of the extracorporeal circuit primed with normal saline solution for 10 minutes, the number of particles 15 to 80 μm in size reached 199 ± 69/mL, 14 times higher than the count before bypass. The application of a Dacron filter (pore size, 5 μm) can remove 87.4% of these particles. Under a light microscope, many foreign microparticles can be observed on the surface of the filter mesh. Another important source of extrinsic particles is silicone oil. Our animal study demonstrated silicone oil emboli in the heart, kidneys, and lungs after CPB with a bubble oxygenator for 2 hours (Fig 9). The roller pump can cause a large number of particles to break off from the compressed silicone rubber tube, an event that occurs most frequently when a new tube is used [10]. The particles 10 to 25 μm in diameter reached their highest number, 1,500/mL, 20 minutes after bypass and decreased markedly after 3 to 4 hours [10].

Intrinsic particles are mainly produced by damage to

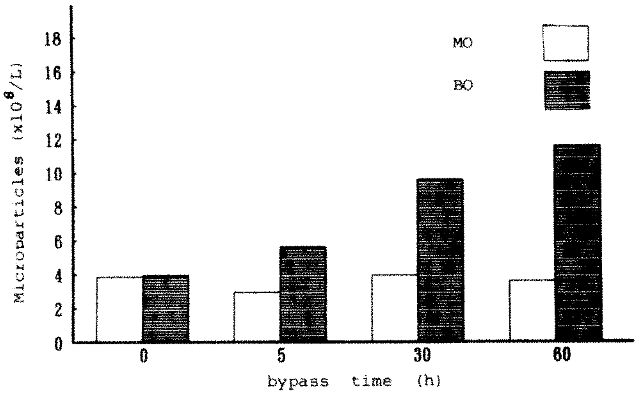


Fig 7. Comparison of number of microparticles produced with a membrane oxygenator (MO) versus a bubble oxygenator (BO) in the cardiopulmonary bypass circuit.

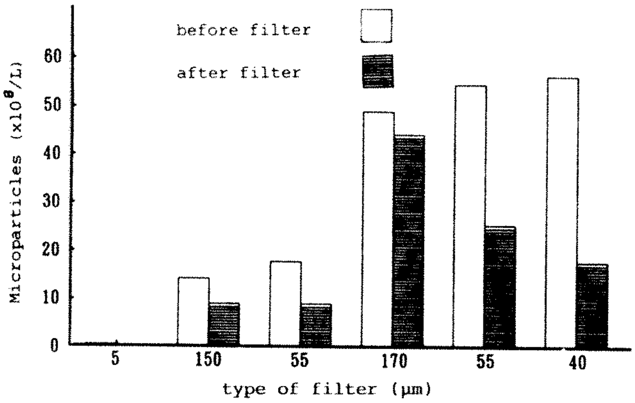


Fig 8. Effectiveness of filters of different pore sizes in reducing microparticle count.

blood elements, denaturation of protein, and aggregation of platelets. We found the major sources of blood-derived particles during extracorporeal perfusion to be (in descending order) banked blood, cardiotomy reservoir, and bubble oxygenator.

In pediatric practice, to prevent excessive hemodilution, blood must often be added to the prime for extracorporeal circulation. We have shown that stored acid-citrate dextrose blood in clinical use contains large quantities of 15- to 80-μm particles, which is correlated with storage time ($r = 0.886$; $p < 0.001$). Of these particles, 94.6% are less than 50 μm in size. Red blood cells, white blood cells, and platelets, especially the last, decrease in number with prolongation of storage time [11].

The main source of microparticles during extracorporeal circulation is the cardiotomy reservoir [12]. Our study indicates that the number of blood microparticles produced by this source is related to the platelet count. The blood microparticles increased up to 5.1 times after passage through the cardiotomy reservoir in the early phase of bypass because of the relatively high platelet count. Our study also showed that the number of particles 15 to 80 μm in size produced by the bubble oxygenator is 1.8 to 3.2 times greater than the number produced with the membrane oxygenator [13–15].

Microparticles produced during extracorporeal circulation can cause embolism in tissues and organs, especially the lungs. The diameter of pulmonary capillaries and small arteries in children is much smaller than in adults [16]. The diameter of a smaller pulmonary artery is 100 to 120 μm and that of a branch, 20 to 25 μm. The capillaries are about 10 to 12 μm in diameter, which allows passage of red blood cells (7 μm). After CPB, pulmonary microcirculation might be obstructed by microparticles and degraded red blood cells, white blood cells, and platelets. We also found obvious changes in the pulmonary ultrastructure with obstruction by polyvinyl chloride particles. The basic pathological process is widespread degeneration of cellular components in the interstitial spaces characterized by edema, rupture of capillary endothelial cells, and denaturation of types I and II epithelial cells. Lysosomal rupture and granules of white blood cells and platelets can be observed in the interstitial spaces. Also, cell and protein exudation is present in alveoli. The degree and the range of histological damage are related not only to the quantity and size of blood microparticles but also to the duration of obstruction of the microcirculation.

There is still controversy regarding the harmful effects of particles smaller than 35 to 40 μm [7]. Microemboli of this size can cause detectable organ damage only when they obstruct a considerable number of small vessels.

To prevent and to reduce tissue damage caused by blood microparticles during CPB, we recommend the following: (1) Avoid or reduce the use of stored blood during CPB. This not only relieves demands on the blood supply but, more importantly, can reduce the complications from transfusion. Currently, we usually do not use banked blood in open heart procedures with CPB in patients weighing more than 10 kg. For patients with a low body weight and hematocrit, fresh blood is used whenever possible. (2) Use a membrane oxygenator to reduce both damage to blood elements and embolism, as

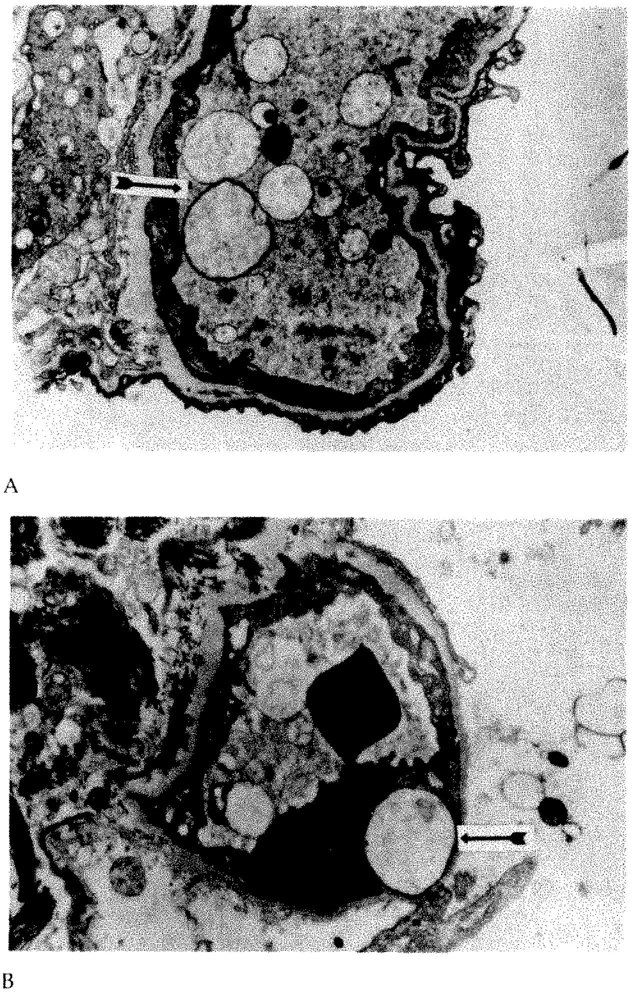


Fig 9. Silicone oil emboli in lungs and heart after cardiopulmonary bypass with a bubble oxygenator for 2 hours: (A) Silicone oil emboli alone (arrow) *and (B) Silicone oil emboli* (arrow) *in the heart. (Both, ×3600 before 11% reduction.)*

this type of oxygenator avoids direct contact of air with blood. In a previous study, we [17] showed that the time of mechanical ventilation was 10 hours shorter in patients with a membrane oxygenator than in those who had a bubble oxygenator. Respiratory secretions and pulmonary complications after operation were also markedly reduced in patients who had a membrane oxygenator ($p < 0.01$). (3) Reduce damage from the cardiotomy system by controlling negative suction pressure. The use of deep hypothermic circulatory arrest in infants may also be of help. (4) Use filters with different pore sizes to remove as many microparticles as possible, as the production of microparticles during CPB cannot be completely eliminated at present. The arterial line filter should provide a large surface area of 650 to 800 $\text{cm} \cdot \text{L}^{-1} \cdot \text{min}^{-1}$, and its pore size should be 40 to 80 μm [7]. Filters with a pore size greater than 150 μm are ineffective in removing microparticles.

We gratefully acknowledge the helpful suggestions and support of Dr Richard A. Jonas, The Children's Hospital, Boston, MA.

References

1. Ratliff NB, Young WG Jr, Hackel BB, et al. Pulmonary injury secondary to extracorporeal circulation. J Thorac Cardiovasc Surg 1973;65:425–32.
2. Allardyce DB, Yoshida SH, Ashmore PG. The importance of microembolism in the pathogenesis of organ dysfunction caused by prolonged use of the pump oxygenator. J Thorac Cardiovasc Surg 1966;52:706–15.
3. Ashmore PG, Cvitek V, Ambrase P. The incidence and effects of particulate aggregation and microembolism in pump-oxygenator systems. J Thorac Cardiovasc Surg 1968;55:691–8.
4. Solis RT, Noon GP, Beall AC Jr, DeBakey ME. Particulate microembolism during cardiac operation. Ann Thorac Surg 1974;17:332–44.
5. Loop FD, Szabo J, Rowlinson RD, Urbanek K. Events related to microembolism during extracorporeal perfusion in man: effectiveness of in-line filtration recorded by ultrasound. Ann Thorac Surg 1976;21:412–20.
6. Clark RE, Deitz DR, Miller JG. Continuous detection of microemboli during cardiopulmonary bypass in animals and man. Circulation 1976;54(Suppl 3):74–8.
7. Edmunds LH Jr, Williams W. Microemboli and the use of filters during cardiopulmonary bypass. In: Utley JR, ed. Pathophysiology and techniques of cardiopulmonary bypass; vol 2. Baltimore: Williams & Wilkins, 1983:101–14.
8. Solis RT, Wright CB, Gibbs MB, et al. Quantitative studies of microaggregate formation in vitro and in vivo. Chest 1974; 65(Suppl 4):44–6.
9. Solis RT, Kennedy PS, Beall AC Jr, et al. Cardiopulmonary bypass microembolization and platelet aggregation. Circulation 1975;52:103–7.
10. Stoney WS, Alford WC Jr, Burrus GR, Glassford DM Jr, Thomas CS Jr. Air embolism and other accidents using pump oxygenators. Ann Thorac Surg 1980;29:336–40.
11. Liu J-F, Su Z-K, Ding W-X. Particle in banked blood and filtration by micropore filters. Chin J Hematol 1990;11:86–7.
12. de Jong JCF, ten Duis HJ, Smit Sibinga CT, Wildevuur CRH. Hematologic aspects of cardiotomy suction in cardiac operations. J Thorac Cardiovasc Surg 1980;79:227–36.
13. Clark RE, Beauchamp RA, Magrath RA, et al. Comparison of bubble and membrane oxygenators in short and long perfusions. J Thorac Cardiovasc Surg 1979;78:655–66.
14. Connell RS, Page US, Bartley TD, Bigelow JC, Webb ML. The effect on pulmonary ultrastructure of Dacron-wool filtration during cardiopulmonary bypass. Ann Thorac Surg 1973;15: 217–29.
15. Bisio JM, Connell RS, Harrison MM. The formation and effect of stored platelet concentrate microemboli on pulmonary ultrastructure. Surg Gynecol Obstet 1982;154:342–7.
16. Tian Niu. Microcirculation. Beijing: Chinese Science Company Publishing, 1980:144–52.
17. Cao D-F, Ding W-X, Su Z-K. Using FuDan AL-2 hollow-fibre membrane oxygenator in undertaking infant cardiac surgery with deep hypothermia and circulatory arrest: a report of 60 cases. J Clin Pediatr 1988;6:362–3.

Complete Cure After a Seemingly Unsuccessful Operation for Wolff-Parkinson-White Syndrome

Peter Rakovec, MD, DSc, Aleš Brecelj, MD, and Igor Zupan, MD

University Medical Center, Ljubljana, Slovenia

A 48-year-old man with Wolff-Parkinson-White syndrome and poorly tolerated atrial fibrillation underwent surgical dissection of an accessory pathway. After operation electrocardiogram revealed a very unfavorable outcome: sinus rhythm with persistence of delta waves alternated with sequences of complete atrioventricular block. Therefore, an early reoperation was planned. Fortunately, in the next days conduction through the accessory pathway and signs of atrioventricular block disappeared. Complete cure was observed during long-term follow-up.

(Ann Thorac Surg 1992;54:1203–5)

Surgical dissection of Kent bundle has been widely accepted in the management of patients with Wolff-Parkinson-White syndrome. In experienced hands the operation is effective in more than 95% of cases and can be performed with negligible mortality [1]. Nevertheless, it is important to assess reliably completeness of accessory pathway ablation, because missed accessory pathways are best treated by early reoperation. In some instances an early evaluation may be an inaccurate predictor of long-term success. Operative damage and edema around the Kent bundle may transiently inhibit conduction through the accessory pathway. An early success, therefore, does not necessarily determine a favorable long-term outcome. On the other hand, an early failure extremely rarely proves to be a long-term success. Such a case forms the basis of this report.

At the University Medical Center in Ljubljana, Slovenia, we have dissected 16 accessory pathways in 15 patients with Wolff-Parkinson-White syndrome since 1988. In 1 of these patients the early postoperative electrocardiographic tracing suggested a very unfavorable outcome. However, the long-term course resulted in a complete cure.

Our patient, a 48-year-old man, underwent operation for Wolff-Parkinson-White syndrome because of atrial fibrillation with fast ventricular response. Four years before the operation tachycardia-induced ventricular dysfunction had developed with symptoms and signs of heart failure. After cardioversion the patient had recovered quickly and had been well until 1990, when atrial fibrillation with fast conduction through the accessory pathway set in again and persisted for 2 weeks. During that period he was medicated with propafenone and aspirin. Cardioversion was required for restoration of sinus rhythm. Left ventricular ejection fraction, assessed by echocardiography and radionuclide ventriculography 3 days after cardioversion, was 0.28, but it increased to 0.55 after 2 months of sinus rhythm. After administration of the cardioactive medication was stopped, an electrophysiologic study revealed ventricular preexcitation due to a left posterior paraseptal accessory pathway.

The patient underwent operation for Wolff-Parkinson-White syndrome after he had given informed consent. The preoperative electrocardiogram showed sinus rhythm and signs of ventricular preexcitation (Fig 1). The intraoperative epicardial mapping confirmed the existence and localization of the accessory pathway. Dissection of the accessory pathway using the endocardial approach was performed under deep hypothermia and cardioplegic arrest. After the warming-up period electrocardiographic tracing revealed a most unfavorable outcome: in addition to the still-present delta wave, conduction through the normal (His-Purkinje) pathway was completely blocked (Fig 2). An immediate reinstitution of cardiopulmonary bypass seemed too dangerous for the patient; therefore, a reoperation after a few days was planned.

Fortunately, 5 hours after operation delta waves and the atrioventricular block completely disappeared from the patient's electrocardiogram. The partial postoperative electrophysiologic study with the use of temporary epicardial wires disclosed exclusive conduction through the normal atrioventricular pathway. The decision to abstain from reoperation was taken.

The patient was followed up for 18 months. He underwent a complete electrophysiologic study 1 year after operation. No conduction through an accessory pathway could be detected, and AH and HV intervals in His bundle electrogram were normal. All electrocardiograms revealed normal QRS complexes during sinus rhythm (Fig 3) as well as during atrial fibrillation.

Comment

Usually only clinical and electrocardiographic data are used for the assessment of the result of accessory pathway

---

Accepted for publication Feb 28, 1992.

Address reprint requests to Dr Rakovec, Clinic of Cardiology, Zaloška 7, 61105 Ljubljana, Slovenia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

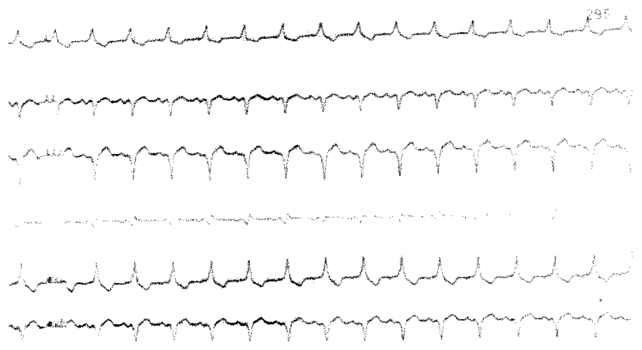


Fig 1. Preoperative electrocardiogram (standard and unipolar limb leads) shows ventricular preexcitation.

dissection. In addition, an early postoperative electrophysiologic study, using temporary epicardial wires, can be performed [2]. This protocol has been recently criticized by Davis and associates [3], who argue that some surgical failures or incomplete results can be overlooked if a complete electrophysiologic study several months after operation is not performed. A temporary disappearance of delta waves after operation with their reappearance in a period of hours or days or even weeks thereafter is not a very rare occurrence. Nevertheless, the absence of delta waves 24 hours after operation is a strong predictor of a successful operation. However, a reverse situation, ie, persistence of signs of preexcitation immediately after operation and disappearance of accessory pathway conduction thereafter, is extremely rare. Davis and associates [3] described 2 such cases among 174 patients undergoing operation. Recently Kuck and Schlüter [4] reported that 2 patients treated with radiofrequency ablation had persistent accessory pathway conduction immediately after treatment, but "spontaneous" conduction block in that pathway developed in them within 3 months of the ablation procedure.

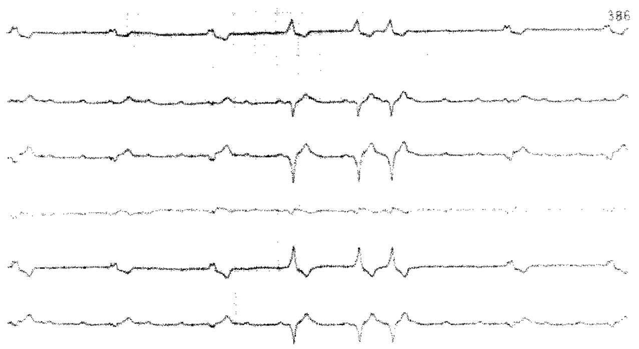


Fig 2. Immediate postoperative electrocardiogram (standard and unipolar limb leads) shows complete atrioventricular block (first three beats) followed by three preexcited beats. At the end of the tracing there are two beats of idioventricular rhythm again. Before and after this tracing there were longer sequences of sinus rhythm with preexcited beats and also longer sequences of complete atrioventricular block.

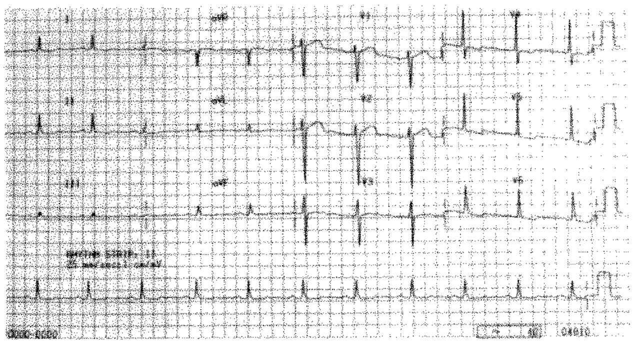


Fig 3. Postoperative electrocardiogram, chronic phase, shows normal sinus rhythm and no preexcitation.

Theoretically, in the process of healing of the surgical incision both possibilities could occur. The acute trauma and edema can temporarily interrupt conduction through the accessory pathway; after healing the conduction can be reinstituted. On the other hand, an incomplete section can allow persistence of conduction immediately after operation. The process of fibrous tissue formation can eventually stop the conduction completely.

In our case the early outcome seemed to be disastrous. Persistence of preexcitation *and* block of the normal pathway conduction is an extremely bad condition. It has been shown that drugs that depress conduction through the normal pathway increase the rate of ventricular response during atrial fibrillation [5, 6]. From our own experience we recall some cases of ventricular fibrillation that developed after verapamil was given to such patients. Thus in patients with atrial fibrillation and Wolff-Parkinson-White syndrome the worst possible surgical outcome is the combination of missed accessory pathway and damaged normal pathway.

Fortunately, in our patient a delayed electrophysiologic study demonstrated a complete abolition of preexcitation and uncompromised atrioventricular conduction through the normal pathway. The patient's ventricular response during atrial fibrillation can be now easily controlled by digoxin and verapamil, drugs that are otherwise contraindicated in patients with ventricular preexcitation.

Our experience with the described patient shows that the outcome of the Wolff-Parkinson-White operation cannot be reliably judged from an early electrocardiogram. However, because an early failure only extremely rarely proves to be a long-term success, we cannot disagree with the authors who advocate treating early failures with an early reoperation.

References

1. Michelson E. Clinical perspectives in the management of the Wolff-Parkinson-White syndrome. Mod Concepts Cardiovasc Dis 1989;58:43–54.
2. McKinnie J, Werner P, Avitall B, Jazayeri M, Akhtar M, Tchou P. Utility of ventriculoatrial conduction patterns in assessing surgical success of accessory pathway ablation. J Cardiovasc Electrophysiol 1991;2:12–20.
3. Davis LM, Johnson DC, Uther JB, et al. What is the best method for assessing the long-term outcome of surgery for

accessory pathways and atrioventricular junctional tachycardias? Circulation 1991;83:528–35.

4. Kuck KH, Schlüter M. Radiofrequency current catheter ablation of accessory atrioventricular pathways. New Trends Arrhyth 1992;8:405–18.
5. Gulamhusein S, Ko P, Klein GJ. Ventricular fibrillation following verapamil in the Wolff-Parkinson-White syndrome. Am Heart J 1983;106:145–7.
6. Byrum CJ, Wahl RA, Behrendt DM, Dick M. Ventricular fibrillation associated with use of digitalis in a newborn infant with Wolff-Parkinson-White syndrome. J Pediatr 1982;101:400–3.

Notice From the American Board of Thoracic Surgery

The American Board of Thoracic Surgery began its recertification process in 1984. Diplomates interested in participating in this examination should maintain a documented list of the operations they performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. (If more than 100 cases occur in 1 year, only 100 need to be listed.) They should also keep a record of their attendance at approved postgraduate medical education activities for the 2 years prior to application. A minimum of 100 hours of approved CME activity is required.

In place of a cognitive examination, candidates for recertification will be required to complete both the general thoracic and cardiac portions of the SESATS IV syllabus (Self-Education/Self-Assessment in Thoracic Surgery). It is not necessary for candidates to purchase SESATS IV booklets prior to applying for recertification. SESATS IV booklets will be forwarded to candidates after their applications have been accepted.

Diplomates whose 10-year certificates will expire in 1995 may begin the recertification process in 1993. This new certificate will be dated 10 years from the time of expiration of the original certificate. Recertification is also open to any diplomate with an unlimited certificate and will in no way affect the validity of the original certificate.

The deadline for submission of applications is May 1, 1993. A recertification brochure outlining the rules and requirements for recertification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Pneumatocele Complicating Hyperimmunoglobulin E Syndrome (Job's Syndrome)

Robert C. Shamberger, MD, Mary Ellen Wohl, MD, Antonio Perez-Atayde, MD, and W. Hardy Hendren, MD

Departments of Surgery, Pediatrics (Division of Pulmonary Medicine), and Pathology, Children's Hospital and Harvard Medical School, Boston, Massachusetts

The case of a boy with hyperimmunoglobulin E syndrome or Job's syndrome is presented to demonstrate the occurrence of pneumatoceles in this syndrome as well as their unusual natural history and failure to spontaneously resolve. Surgical resection was required for two complications in this patient, persistent bronchopleural fistula and a pulmonary abscess that destroyed one lung and required pneumonectomy. Pathologic examination of the specimens demonstrated the wall of the cysts consisted of granulation tissue with chronic active inflammation surrounded by infarcted pulmonary parenchyma with coagulative necrosis. The mechanism responsible for increased immunoglobulin E production in this syndrome is unknown, as is the manner in which elevated immunoglobulin E levels impair normal immune function.

(Ann Thorac Surg 1992;54:1206–8)

Hyperimmunoglobulin E syndrome (HIE) or Job's syndrome is a complex disorder characterized by extremely high levels of serum immunoglobulin (Ig) E, recurrent infections (particularly resulting from *Staphylococcus aureus* and fungus), and chronic dermatitis. We report an unusual case in which a boy with HIE presented with two major complications of pneumatoceles, each of which required surgical intervention. The unusual natural history of pneumatoceles in patients with this syndrome is stressed as well as the need for surgical intervention when complications occur.

The patient was the product of an uncomplicated pregnancy. He had an episode of tachypnea in the first day of life for which a chest radiograph was obtained. It was completely normal. He had multiple episodes of otitis media and a papulovesicular rash on his face and neck during his first 3 years of life. When he was 3 years old a tonsillectomy and adenoidectomy were performed, which produced only temporary relief of his recurrent middle ear infections. Tests for cystic fibrosis (sweat chloride) were negative, and initial Ig levels were within normal limits (IgG, 9.7 g/L; IgA, 2.38 g/L; and IgM, 0.9 g/L). At age 5 years he had a spontaneous pneumothorax resulting from rupture of a previously unrecognized pneumatocele in the right upper lobe, which was believed initially to be an apical bleb on the chest radiograph. A right upper lobectomy was performed when the bronchopleural fistula did not resolve with tube thoracostomy drainage. At thoracotomy a single large cyst was identified in the right upper lobe. Pathologic examination demonstrated the cyst lacked an epithelial lining and had several bronchi opening directly into the cyst. Chronic active inflammation was present in the wall of the cyst, and there was arteritis of adjacent medium-sized vessels. He did well after this resection, but bronchospastic pulmonary disease developed and was treated with theophylline.

When he was 8 years old the diagnosis of HIE was established as the cause of his recurrent episodes of otitis media and *S aureus* infections in the skin. The serum IgE level was 5,100 U/mL. He was then treated long-term with dicloxacillin. At 10 years of age a pneumatocele was first identified in the right middle lobe, and at 10½ years of age a pneumatocele developed in the right lower lobe after a *Haemophilus influenzae* pneumonia. These pneumatoceles were followed up expectantly and remained thin-walled and stable in size until he was 19 years of age, when he was seen with an abscess in the pneumatocele in the right lower lobe (Fig 1). Initial attempts at another institution to manage the infection by antibiotics and subsequently by percutaneous catheter drainage of the pneumatocele were unsuccessful, and the area of involvement progressively enlarged (Fig 2). Pulmonary function tests and radioisotope perfusion and ventilation scans demonstrated no function of the entire right lung. A right pneumonectomy was performed.

Pathologic examination revealed extensive necrotizing, suppurative, predominantly eosinophilic bronchopneumonia with necrotizing bronchiolitis and suppurative bronchiectasis with partial destruction of bronchiolar epithelium (Fig 3). The pneumatocele had no epithelial lining, and the wall was made of granulation tissue, necrosis, and marked inflammation and appeared sharply demarcated from the compressed lung parenchyma. The interior of the cyst contained necrotic amorphous material with numerous Charcot-Leyden crystals, inflammatory cells with a predominance of eosinophils, and numerous septated branching fungi. *Aspergillus fumigatus* was cultured from the cyst contents. The *Aspergillus* was thought to represent colonization of the pneumatocele, however,

---

Accepted for publication Feb 28, 1992.

Address reprint requests to Dr Shamberger, Department of Surgery, Children's Hospital, 300 Longwood Ave, Boston, MA 02115.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

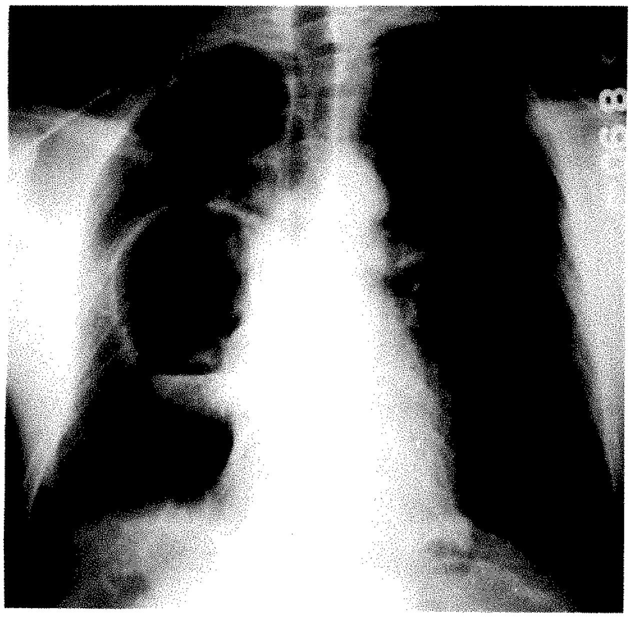


Fig 1. Chest radiograph obtained when the patient was seen with acute infection of the pneumatocele. The wall of the pneumatocele was thickened, and a fluid level was present.

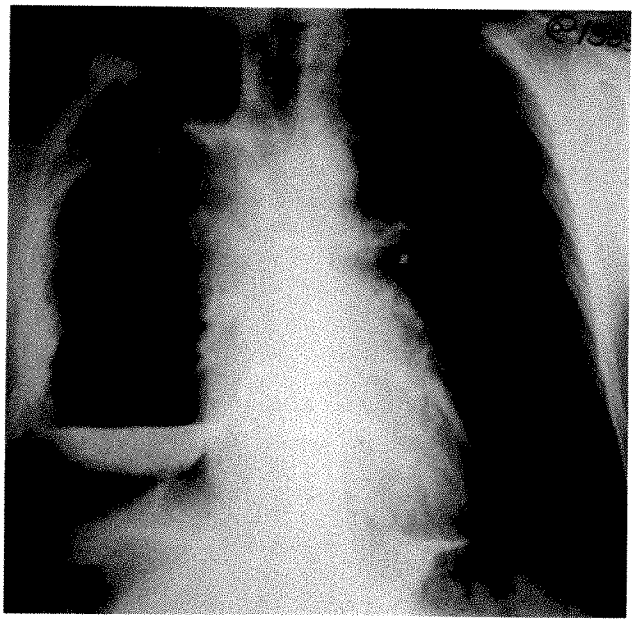


Fig 2. Chest radiograph taken 7 weeks after Figure 1 demonstrates progressive enlargement of the pneumatocele and destruction of surrounding pulmonary parenchyma.

as there was no histologic evidence of invasive infection. In areas the cyst contained the outlines of infarcted pulmonary parenchyma with coagulative necrosis. Adjacent to the cyst occasional necrotizing active arteritis with organizing thrombosis was noted (Fig 4). The pneumatocele extended very close to the lower lobe bronchus.

He has done well in the 15 months following this resection. He continues to receive dicloxacillin, and intravenous γ-globulin has been added to his treatment.

Comment

Hyperimmunoglobulin E syndrome is an extremely rare disorder first reported by Davis, Schaller, and Wedgwood in 1966 [1]. Their patients had recurrent sinopulmonary infections, dermatitis, and *S aureus* abscesses. These "cold abscesses" were notable for their lack of surrounding inflammation. Davis and associates suggested the term *Job's syndrome* to describe their patients based on the Book of Job 2:7, "So went Satan forth from the presence of the Lord, and smote Job with some boils from the sole of his feet unto his crown." Buckley and co-workers [2] linked these clinical findings with markedly elevated serum IgE levels and coarse facies. The mechanisms responsible for increased IgE production in HIE are unknown. A decreased population of suppressor $CD8^+$ lymphocytes has been demonstrated in this syndrome [3, 4]. The elevated IgE levels have been postulated to reflect a T-cell imbalance resulting in T-cell activation and a deficiency of suppressor T cells to inhibit IgE production. It has recently been demonstrated that the cells producing IgE in HIE are largely independent of cell to cell interactions and

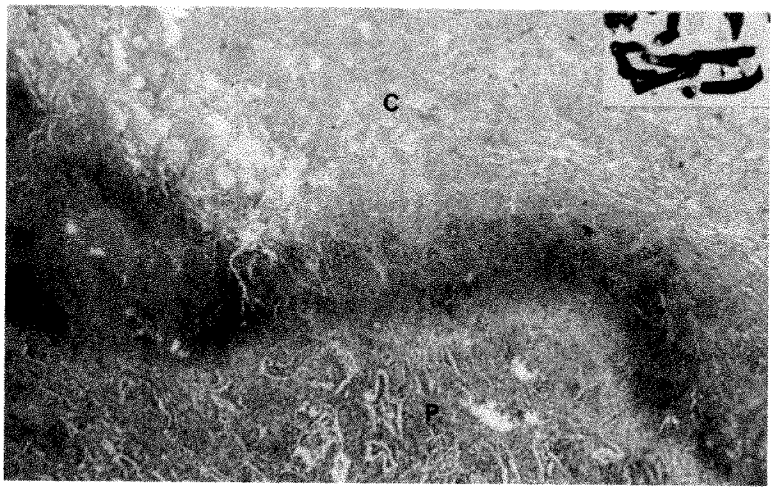


Fig 3. Part of the large pneumatocele outlined by a wall of inflammation and necrosis. The cyst contents are made up of coagulative necrotic pulmonary parenchyma, cellular and inflammatory debris, and fungal colonies. (Hematoxylin and eosin; ×100 before 20% reduction.) The inset displays branching septate Aspergillus fumigatus *stained with methenamine silver (×1000 before 20% reduction). (C = cyst, P = pulmonary parenchyma.)*

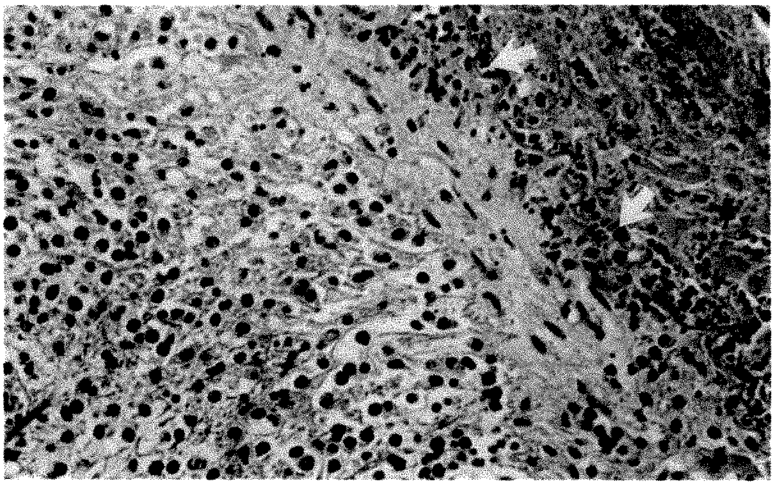


Fig 4. Wall of medium-sized artery showing necrotizing mixed inflammation with lymphocytes, plasma cells, neutrophils, and eosinophils. The inner elastic membrane appears focally disrupted (arrows). *(Hematoxylin and eosin; ×400 before 20% reduction.)*

are not responsive to the normal regulatory signals such as γ-interferon and interleukin G [5]. The patients produce high levels of IgE directed against *S aureus* and other organisms with a deficit in synthesis of IgG antibody against these organisms [6]. The neutrophils are normal in number and can ingest and kill bacteria normally, but their function and chemotaxis appears to be impaired by the extremely high levels of IgE. Patients with HIE are particularly susceptible to infections of *S aureus* and *Candida albicans*, but also to other suppurative infections from *H influenzae, Streptococcus pneumoniae, Escherichia coli,* and *Pseudomonas*. Deep-seated infections other than pneumonias are unusual. In a previous report 6 of 13 patients had lobectomies performed for recurrent hemoptysis secondary to bronchiectasis and recurrent pneumonias [7].

Staphylococcal pneumonia in the era before antibiotics frequently produced pneumatoceles [8, 9]. These would generally resolve with fibrosis and did not persist. In our patient the middle and lower lobe pneumatoceles were present over a 9-year period with a gradual increase in their size. Pneumatoceles have been reported previously in other patients with HIE [7, 10, 11], but the natural history of the pneumatoceles has not been well described. In a remarkable series of 11 patients with HIE reported by Merten and associates [11], all had "lung cysts" and in 4 patients they were multiple. In 5 patients the "cysts" were reported to have spontaneously resolved after continuous antibiotic therapy. No evidence of chronic infection was seen in these patients. In the remaining 6 patients the "cysts" persisted, and in 4 resections were performed.

This case is presented to increase recognition of the occurrence of pneumatoceles in HIE as well as to establish the frequent failure of spontaneous resolution despite long-term observation. Pathologic examination demonstrated necrosis of the surrounding pulmonary parenchyma with necrotizing bronchiolitis and arteritis as the mechanism of rapid increase in size of the lesion. In this patient the T-cell number and measurable function were normal as was the antibody response when assessed 6 months before he was seen with the pulmonary abscess. Thus, in the face of normal immune parameters, the pneumatocele persisted and became infected. This is the second report of *Aspergillus* colonization complicating the course of a pneumatocele in HIE [12].

We thank Raif S. Geha, MD, of the Department of Immunology for his assistance in the preparation of the manuscript.

References

1. Davis SD, Schaller J, Wedgwood RJ. Job's syndrome: recurrent, "cold," staphylococcal abscesses. Lancet 1966;1:1013–5.
2. Buckley RH, Wray BB, Belmaker EZ. Extreme hyperimmunoglobulinemia E and undue susceptibility to infection. Pediatrics 1972;49:59–70.
3. Katona IM, Tata G, Scanlon RT, Bellanti JA. Hyper IgE syndrome: a disease with suppressor T cell deficiency. Ann Allergy 1980;45:295–300.
4. Geha RS, Reinherz E, Leung D, McKee KT Jr, Schlossman S, Rosen FS. Deficiency of suppressor T cells in the hyperimmunoglobulin E syndrome. J Clin Invest 1981;68:783–91.
5. Vercelli D, Jabara HH, Cunningham-Rundles C, et al. Regulation of immunoglobulin (Ig)E synthesis in the hyper-IgE syndrome. J Clin Invest 1990;85:1666–71.
6. Leung DYM, Ambrosino DM, Arbeit RD, et al. Impaired antibody responses to hyperimmunoglobulinemia E syndrome. J Allergy Clin Immunol 1988;81:1082–7.
7. Donabedian H, Gallin JI. The hyperimmunoglobulin E recurrent-infection (Job's) syndrome: a review of the NIH experience and the literature. Medicine 1983;62:195–208.
8. Hendren WH III, Haggerty RJ. Staphylococcic pneumonia in infancy and childhood: analysis of seventy-five cases. JAMA 1958;168:6–16.
9. Sabiston DC Jr, Hopkins EH, Cooke RE, Bennett IL Jr. The surgical management of complications of staphylococcal pneumonia in infancy and childhood. J Thorac Cardiovasc Surg 1959;38:421–34.
10. Geha RS, Leung DYM. Hyper immunoglobulin E syndrome. Immunodefic Rev 1989;1:155–72.
11. Merten DF, Buckley RH, Pratt PC, Effmann EL, Grossman H. Hyperimmunoglobulinemia E syndrome: radiographic observations. Radiology 1979;132:71–8.
12. Lui RC, Inculet RI. Job's syndrome: a rare cause of recurrent lung abscess in childhood. Ann Thorac Surg 1990;50:992–4.

Surgical Treatment of Postinfarction Ventricular Septal Defect With Aortic Stenosis

Lauren R. Boglioli, BS, Thomas A. Traill, MRCP, Alfred S. Casale, MD,
Bruce A. Reitz, MD, and Duke E. Cameron, MD

Divisions of Cardiac Surgery and Cardiology, The Johns Hopkins Hospital, Baltimore, Maryland

A 69-year-old man with an acute postinfarction ventricular septal defect was also found to have aortic stenosis. Successful management required closure of the postinfarction ventricular septal defect and replacement of the stenotic aortic valve. The contribution of aortic stenosis to the cause of the infarction and the postinfarction ventricular septal defect, as well as the implications for surgical management, are discussed.

(Ann Thorac Surg 1992;54:1209–11)

Postinfarction ventricular septal defect (PIVSD), first described by Latham in 1846 [1], accounts for approximately 1% of all deaths associated with acute myocardial infarction. When treated nonoperatively, it carries a 65% mortality rate within 2 weeks of perforation and 86% within 2 months [2]. Since Cooley and associates' [3] 1957 report of the first successful surgical repair of PIVSD, surgical therapy has become the treatment of choice for this condition. In the case presented herein, PIVSD occurred with aortic stenosis. High intraventricular pressure from aortic valve stenosis probably contributed to septal rupture, and aortic valve replacement was essential to successful repair.

A 69-year-old man was hospitalized for unremitting retrosternal chest pain of 5 hours duration. The patient had a 15-year history of mild hypertension, a 75-pack-year history of cigarette smoking, and a family history of coronary artery disease. Eighteen months before admission, aortic stenosis was suspected by physical examination. No history of myocardial infarction, diabetes mellitus, or chronic obstructive pulmonary disease was elicited.

On admission the temperature was 37.1°C, the pulse was 94 beats/min, and respirations were 18/min. The blood pressure was 160/100 mm Hg. A grade 2–3/6 systolic ejection murmur was heard at the apex and radiated to the axilla and left sternal border. An electrocardiogram showed ST elevation in V_2 through V_4 and Q waves in V_5 and V_6. A Killip II anteroseptal infarction was diagnosed, and the creatine kinase level peaked at 1,243 U/L. An echocardiogram revealed a thickened stenotic aortic valve. There was moderately reduced left ventricular function with anteroapical akinesis; the ejection fraction was estimated at 0.30.

Five days after admission, the patient experienced further cardiac pain relieved by trinitroglycerin. The creatine kinase level rose to 429 U/L, suggesting reinfarction. The following day the lung bases had fine rales and the blood pressure decreased to 90/60 mm Hg. A Swan-Ganz catheter revealed a pulmonary capillary wedge pressure of 20 mm Hg, central venous pressure of 8 mm Hg, and cardiac output of 5.1 L/min.

The next day, a new pansystolic murmur was heard. The blood pressure fell to 75/50 mm Hg and the pulmonary capillary wedge pressure rose to 37 mm Hg. The patient was oliguric and unresponsive to intravenous fluid therapy. An intraaortic balloon pump was inserted into the right common femoral artery, and the patient was transferred to The Johns Hopkins Hospital.

A repeat Doppler echocardiographic examination confirmed an anteroapical ventricular septal defect and an aortic valve gradient of 30 to 40 mm Hg. Emergency coronary arteriogram showed right coronary artery dominance with occlusion of the proximal left anterior descending coronary artery (Fig 1) and no other coronary artery disease. The aortic valve appeared heavily calcified.

Hemoglobin-oxygen saturations were 99% in the aorta, 38% in the right atrium, and 79% in the pulmonary artery. The calculated pulmonary-to-systemic blood flow ratio was 3.6:1 and the cardiac output approximately 2.3 L/min. Calculated aortic valve area was 0.65 cm^2. Because of severe hemodynamic compromise, the patient was referred for emergency surgical intervention.

At sternotomy, the heart was discolored, sluggish, and dilated. Hypothermic (25°C) cardiopulmonary bypass was instituted and the heart was arrested with potassium cardioplegia. The aortic valve was tricuspid, severely calcified, sclerotic, and stenotic. There were several unusual calcium excrescences resembling snowflakes, which were loosely adherent to the valve leaflets. The valve was replaced with a 25-mm porcine bioprosthesis. Through a vertical anterior wall ventriculotomy, Dacron patch closure of the anteroapical ventricular septal defect was performed. The intraaortic balloon pump was left in place, and the patient was weaned from cardiopulmonary bypass with moderate-dose dobutamine (4 $\mu g \cdot kg^{-1} \cdot min^{-1}$). The patient required epicardial atrioventricular pacing for heart block.

The patient made a steady hemodynamic recovery; by the 4th postoperative day, the intraaortic balloon pump

---

Accepted for publication March 3, 1992.

Address reprint requests to Dr Cameron, The Johns Hopkins Hospital, 600 N Wolfe St, Blalock 618, Baltimore, MD 21205.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

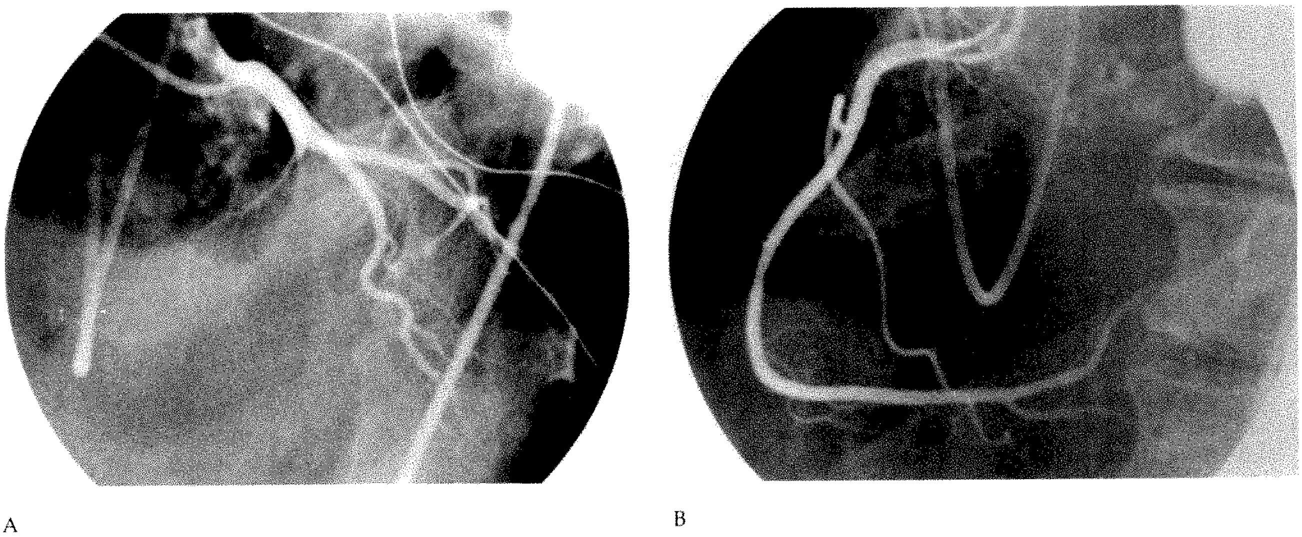


Fig 1. Coronary angiograms of patient with postinfarction ventricular septal defect and aortic stenosis: (A) left anterior oblique projection of left coronary injection shows occlusion of proximal left anterior descending coronary artery and calcification of aortic valve; (B) left anterior oblique projection of right coronary artery injection shows a normal vessel.

was removed and by 1 week, normal sinus rhythm returned. The postoperative course was complicated by recurrent pleural effusions, which were treated by thoracentesis. A cricothyroidotomy was required on the 16th postoperative day for ventilatory insufficiency, and the patient had several bouts of pulmonary sepsis. He was eventually weaned from ventilatory and inotropic support. He underwent complete physical rehabilitation and was discharged 3 months after operation. Nearly 3 years later, his functional capacity is good; he can climb two flights of stairs without dyspnea, does yard work, and has resumed full-time employment as a retailer.

Comment

Acquired ventricular septal defect is an uncommon complication of myocardial infarction. Risk factors include first myocardial infarction, large transmural infarction, complete acute occlusion of a coronary artery, limited collateral flow, alterations of septal geometry, late infarct extension, left ventricular hypertrophy, and hypertension [4]. Ventricular septal rupture usually occurs 4 to 12 days after myocardial infarction, when myocardial necrosis renders the septum weakest [3, 5]. Septal perforation is diagnosed by sudden onset of a new harsh pansystolic murmur, usually loudest along the left sternal border and frequently radiating to the axilla. A thrill is often noted. Chest pain sometimes occurs at the time of septal rupture. The diagnosis can be confirmed at bedside by "step-up" in the hemoglobin-oxygen saturation between right atrium and pulmonary artery. Postinfarction ventricular septal defect is often accompanied by rapid development of congestive failure, hypotension, pulmonary edema, altered mental status, and renal failure.

There is substantial mortality associated with the left-to-right shunt imposed on damaged myocardium with poor functional reserve. Risk factors for mortality in PIVSD have been identified and include right ventricular and septal dysfunction, inferior versus anterior wall infarction, large defect, older patient age, early septal rupture after infarction, development of cardiogenic shock, and mean right atrial pressure greater than 12 mm Hg.

Medical therapy is usually ineffective for PIVSD. Intraaortic balloon counterpulsation is a temporizing measure that permits hemodynamic stabilization for preoperative cardiac catheterization [6]. According to Gold and associates [7], the peak improvement from intraaortic balloon pumping occurs within 24 hours and is not enhanced by prolonged balloon support. Surgical closure is currently the only accepted definitive treatment for PIVSD [5]. The appropriate interval between rupture and surgical intervention has been controversial; recently, superior results have been reported with early repair [8]. Delay of operation results in multisystem failure in the majority of patients.

The patient presented here had an unusual combination of aortic stenosis and PIVSD. The coronary lesion responsible for the infarction was probably atherosclerotic, but loose calcium excrescences on the aortic valve raised the possibility of embolism. The patient underwent emergency aortic valve replacement and closure of the ventricular septal defect. Elevated left ventricular pressure from aortic stenosis probably contributed to septal rupture. Septal hypertrophy is a recognized risk factor for PIVSD and was probably not protective against septal rupture. We believe that successful surgical outcome was dependent on recognition and treatment of both lesions. Had aortic stenosis not been relieved, persistent high left ventricular pressures might have led to ventricular septal defect patch dehiscence or postoperative left ventricular failure.

This case report illustrates the importance of treating concurrent valve lesions that may predispose to septal rupture after infarction and jeopardize the security of patch repair.

References

1. Latham PM. Lectures on subjects connected with clinical medicine, comprising diseases of the heart. vol 2. London: Longman, Brown, Green, and Longmans, 1846:168–76.
2. Oyamada A, Queen FB. Spontaneous rupture of the interventricular septum following acute myocardial infarction with some clincopathological observations on survival in five cases. Presented at the Pan-Pacific Pathology Congress, Tripler US Army Hospital, Honolulu, HI, Oct 12, 1961. Cited in Murphy TE, DeBoer A. Surgical management of ventricular septal defects following myocardial infarction. In: Moran JM, Michaelis LL, eds. Surgery for the complications of myocardial infarction. New York: Grune & Stratton, 1980:191–210.
3. Cooley DA, Belmonte BA, Zeis LB, Schnur S. Surgical repair of ruptured interventricular septum following acute myocardial infarction. Surgery 1957;41:930–7.
4. Radford MJ, Johnson RA, Daggett WM, et al. Ventricular septal rupture: a review of clinical and physiologic features and an analysis of survival. Circulation 1981;64:545–53.
5. Heitmiller R, Jacobs ML, Daggett WM. Surgical management of postinfarction ventricular septal rupture. Ann Thorac Surg 1986;41:683–91.
6. Baillot R, Pelletier C, Trivino-Marin J, Castonquay Y. Postinfarction ventricular septal defect: delayed closure with prolonged mechanical circulatory support. Ann Thorac Surg 1983;35:138–42.
7. Gold HK, Leinbach RC, Sanders CA, Buckly MJ, Mundth ED, Austen WG. Intraaortic balloon pumping for ventricular septal defect or mitral regurgitation complicating acute myocardial infarction. Circulation 1973;47:1191–6.
8. Gaudiani VA, Miller DC, Stinson EB, et al. Posttinfarction ventricular septal defect: an argument for early operation. Surg 1981;89:48–55.

Pleural Liposarcoma Presenting With Respiratory Distress and Suspected Diaphragmatic Hernia

Francis Carroll, MD, Marshall D. Kramer, MD, Anthony J. Acinapura, MD,
Patricia A. Tietjen, MD, Ira Wagner, MD, Stanley Oiseth, MD, and Fred Smith, MD

Departments of Surgery, Medicine, and Pathology, St. Vincent's Hospital and Medical Center, New York, New York, and New York Medical College, Valhalla, New York

A young woman with a history of diaphragmatic hernia presented to the hospital in respiratory distress and in premature labor. Her admission chest roentgenogram showed opacification of the left hemithorax, and her arterial blood gas analysis revealed hypoxemia. Emergency cesarean section and exploratory left thoracotomy were carried out; a large tumor occupied the left side of the chest, and pneumonectomy was performed. No diaphragmatic hernia was present. A pathologic diagnosis of primary liposarcoma was made.

(Ann Thorac Surg 1992;54:1212–3)

Liposarcomas are among the most common malignant mesenchymal tumors occurring in adults. Primary intrathoracic liposarcomas, however, are decidedly rare, as most liposarcomas arise in the extremities or retroperitoneum. The following is a case report of a liposarcoma arising from the pulmonary ligament in a young pregnant woman.

A 23-year-old woman with a history of left diaphragmatic hernia, repaired 16 months earlier, was transferred to our institution in respiratory distress and in premature. On arrival, she complained of shortness of breath and abdominal pain. On physical examination, she was tachycardic and tachypneic. She had a temperature of 38.1°C and blood pressure of 140/90 mm Hg. She had decreased breath sounds on the left side. The abdomen was distended, consistent with a gravid uterus of 32 to 33 weeks gestation, and an upper midline vertical abdominal incision was noted. Vaginal examination revealed a cervix that was 100% effaced and 4 cm dilated. The initial chest roentgenogram revealed opacification of the left hemithorax and mediastinal shift to the right (Fig 1).

An arterial blood gas analysis was obtained: pH = 7.46, carbon dioxide tension = 29 mm Hg, HCO_3 = 20, oxygen tension = 51 mm Hg, and oxygen saturation = 88%. A complete blood count revealed a white blood cell count of $13.1 \times 10^9/L$ and a hemoglobin level of 124 g/L. A computed tomographic scan of the chest was performed (Picker 1200) without intravenous or oral contrast (Fig 2). This demonstrated an opacified left hemithorax with a shift of the heart and mediastinal structures to the right. The scan was interpreted as recurrent left diaphragmatic hernia.

A preoperative diagnosis of recurrent left diaphragmatic hernia with secondary hypoxia and preterm labor was made. The patient was brought to the operating room, where cesarean section was performed. A left thoracotomy was next performed; a bulky, encapsulated, lobulated tumor was encountered that filled the entire hemithorax. A thoracoabdominal extension was made; no hernia was encountered and all abdominal viscera were found intraabdominally. The lower pulmonary lobe was replaced, and the upper lobe appeared rudimentary. A pneumonectomy was carried out. Her postoperative course was uncomplicated, and she was discharged 2 weeks postoperatively with a healthy baby boy.

The pathologic specimen was received in two parts, which measured 29 × 15 × 15 cm and 21 × 12 × 8 cm and weighed 4,460 g total. The specimens were multilobular and well-encapsulated; the larger fragment was continuous with the inferior ligament of the left lung. Cross-section revealed yellow areas of fat, areas of clear gelatinous tissue, cartilaginous areas, and several firm white nodules (Fig 3). Microscopic sections showed a predominantly lipoblastic neoplasm with foci of anaplastic bizarre multinucleated giant cells. The pathologic diagnosis was liposarcoma, mixed-type. Extensive infiltration of the lower lobe parenchyma was present.

Comment

Liposarcomas account for 10% to 12% of soft tissue tumors in adults. The peak incidence is in the sixth decade, although there have been 17 reported cases in children [1]. There is a slight male predominance, and these tumors can grow to an extremely large size. Liposarcomas generally arise in the extremities and the retroperitoneum. Less common sites are the inguinal and paratesticular regions, the breast, and chest wall. Primary intrathoracic liposarcomas are uncommon. Cases of mediastinal, pulmonary, and pericardial origin and of origin from the interatrial septum have been reported. Seven liposarcomas arising from the pleura have been previously reported [2–4].

Accepted for publication March 6, 1992.

Address reprint requests to Dr Kramer, O'Toole, Suite 423, 36 Seventh Ave, New York, NY 10011.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

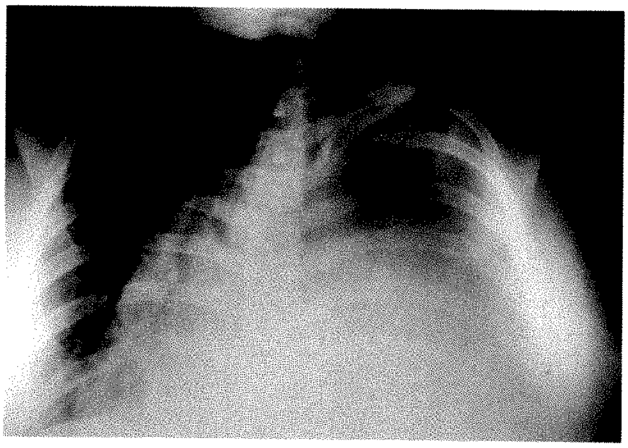


Fig 1. Initial chest roentgenogram shows opacification of the left hemithorax and mediastinal shift to the right.

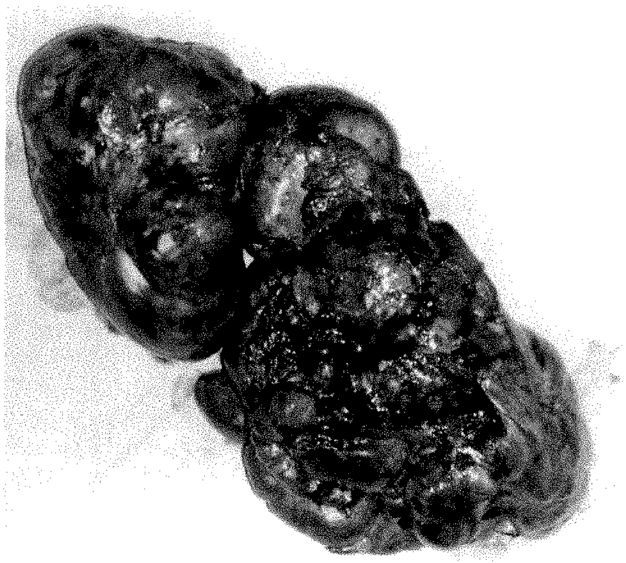


Fig 3. Gross specimen photographed in the operating room.

The case reported here is that of an extremely large liposarcoma arising from the inferior pulmonary ligament. Of the previously reported pleural liposarcomas, five occurred in male patients ranging in age from 19 to 61 years. Five involved the left lung and two involved the right lung. In the 5 cases where weights were available, all were greater than 900 g. These tumors reach large proportions because they grow insidiously in areas that are not accessible to physical examination. The presenting complaints are nonspecific and include pain, dyspnea, cough, and hemoptysis. Anorexia and weight loss are late symptoms.

Liposarcomas can be divided into four basic histologic categories: myxoid, well-differentiated, round cell, and pleomorphic. This system, as described by Enzinger and Winslow, correlates well with prognosis. The overall 5-year survival rate for liposarcomas as a group varies from 57% to 70%, but the myxoid and well-differentiated liposarcomas have much higher survival rates than the round cell and pleomorphic types [5]. In general, recurrence of a mixed pattern liposarcoma may be expected in approximately 50% of cases [6].

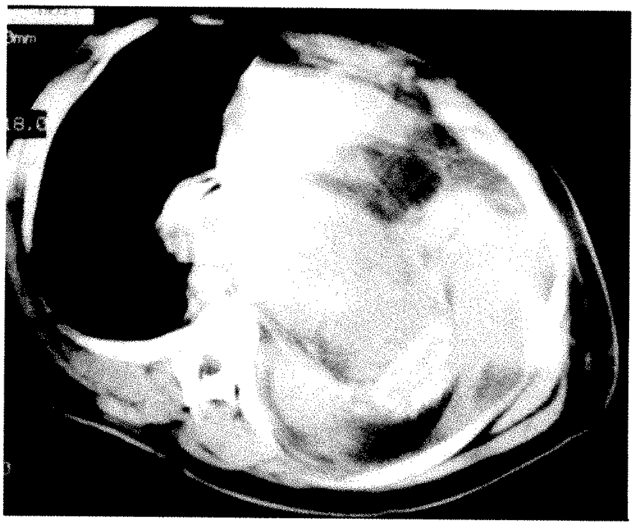


Fig 2. Computed tomographic scan of the chest shows multiple soft tissue densities and a hyperdense area, consistent with prosthetic material.

The treatment of choice is radical excision because local recurrence is common. Several series have shown an increased survival with a combination of operation and radiotherapy [7]. In cases that are inoperable, radiotherapy should be tried.

In conclusion, a young woman presented with dyspnea, hypoxemia, and preterm labor caused by a massive liposarcoma that arose from the inferior pulmonary ligament and filled the entire left hemithorax. Preoperatively, the history of diaphragmatic hernia was misleading, and the diagnosis was made intraoperatively. Postoperatively, she received adjuvant radiotherapy and is currently well and free of disease after 16 months. She has been followed up clinically and with serial computed tomographic scans.

References

1. Schmookler BM, Enzinger FM. Liposarcoma occurring in children. Cancer 1983;52:567–74.
2. Gupta RK, Paolini FA. Liposarcoma of the pleura: report of a case. Am Rev Respir Dis 1967;95:298–304.
3. McGregor DH, Dixon AY, Moral L, Kanabe S. Liposarcoma of pleural cavity with recurrence as malignant fibrous histiocytoma. Ann Clin Lab Sci 1987;17:83–92.
4. Munk PL, Muller NL. Pleural liposarcoma: CT diagnosis. J Comput Assist Tomogr 1988;12:709–10.
5. Sawamura K, Hashimoto T, Nanjo S, et al. Primary liposarcoma of the lung: report of a case. J Surg Oncol 1982;19:243–6.
6. Evans HL. Liposarcoma: a study of 55 cases with a reassessment of its classification. Am J Surg Pathol 1979;3:507–23.
7. Celik C, Karakousis CP, Moore R, Holyoke ED. Liposarcomas: prognosis and management. J Surg Oncol 1980;14:245–9.

Retrograde Coronary Sinus Cardioplegia in the Presence of Persistent Left Superior Vena Cava

David M. Shahian, MD

Department of Thoracic and Cardiovascular Surgery, Lahey Clinic Medical Center, Burlington, Massachusetts

Administration of retrograde cardioplegia is hampered by the presence of a persistent left superior vena cava, which results in excessive runoff of solution into the persistent left superior vena cava and the right atrium. Technical modifications are described that permitted aortic valve replacement to be performed in a patient with persistent left superior vena cava using only retrograde cardioplegia.

(Ann Thorac Surg 1992;54:1214–5)

Retrograde cardioplegia through the coronary sinus is a valuable new adjunct to myocardial protection [1]. The procedure is particularly useful when the native coronary arteries are totally occluded or during operations, such as aortic valve or mitral valve replacement, in which cardioplegia can be administered either periodically or continuously without disruption of the procedure. We recently encountered a patient in whom retrograde cardioplegia was highly desirable but who had a congenital anomaly that created technical problems. Our management of this patient's condition is described.

A 66-year-old woman had a 2-year history of chest pain and dyspnea on exertion. Findings on physical examination were consistent with aortic stenosis. Results of echocardiography and cardiac catheterization revealed critical aortic stenosis with a calculated valve area of 0.5 cm^2. The coronary arteries were normal although the left and right main coronary ostia were small. The patient was referred for aortic valve replacement. After sternotomy, no innominate vein could be found. On elevation of the heart, a persistent left superior vena cava was found that drained into a greatly dilated 3-cm coronary sinus. Because this anomaly would presumably prevent occlusion by the usual self-inflating balloon catheter (Research Medical, Inc, Salt Lake City, UT), which is 1.8 cm when maximally inflated, retrograde cardioplegia was thought to be impractical.

The patient was placed on cardiopulmonary bypass and cooled, and the heart was arrested using antegrade cold blood cardioplegia. Oblique aortotomy was performed, and a bicuspid aortic valve was excised. Both coronary ostia were small and resembled slits, and attempts to cannulate the coronary ostia were unsuccessful, even with the smallest cardioplegia perfusion cannulas. Retrograde cardioplegia thus became a necessity despite the presence of a persistent left superior vena cava and the greatly dilated coronary sinus ostium. A cotton umbilical tape and tourniquet were placed around the left superior vena cava and were left loose. A Research Medical retroplegia catheter was inserted through a pursestring suture in the right atrium into the coronary sinus. The left superior vena caval tourniquet was tightened only during periods of administration of retrograde cardioplegia. At the same time, finger pressure was used at the junction of the inferior vena cava and the right atrium to occlude the coronary sinus ostium. Effective coronary sinus pressures of about 40 mm Hg were obtained, and myocardial protection was excellent. Administration of retrograde cardioplegia was continued periodically every 20 to 30 minutes throughout the remainder of the operation. The patient had an uneventful postoperative recovery with no evidence of myocardial injury.

Comment

A persistent left superior vena cava secondary to a residual left anterior cardinal vein occurs in 0.3% to 0.5% of the general population, in 2% to 4% of patients with congenital heart disease, and in up to 40% when such patients have abnormal situs [2, 3]. This abnormality may be discovered incidentally at the time of cardiac operation. The primary findings are an absent or atretic innominate vein and a hugely dilated coronary sinus into which most persistent left superior venae cavae drain. When an intraatrial procedure is planned, the persistent left superior vena cava may be cannulated directly external to the atrium or through the coronary sinus os. To prevent cerebral edema, the persistent left superior vena cava should not be occluded for a prolonged period. When single venous cannulation is planned without intraatrial operation, modification of technique is usually not required.

The presence of a dilated coronary sinus secondary to persistent left superior vena cava can cause technical problems when retrograde cardioplegia is desired. Runoff of cardioplegic solution from the coronary sinus into the persistent left superior vena cava must be prevented. This can be accomplished using intermittent tourniquet occlusion of the persistent left superior vena cava during administration of cardioplegia. Runoff of cardioplegic solution from the dilated coronary sinus os into the right atrium is achieved by digital compression of the os, a method previously described by Drinkwater and associates [1] as an occasional adjunct to achieve adequate coronary sinus pressure during delivery of retrograde cardioplegia. With use of these techniques, it was possible

---

Accepted for publication March 12, 1992.

Address reprint requests to Dr Shahian, Department of Thoracic and Cardiovascular Surgery, Lahey Clinic Medical Center, 41 Mall Rd, Burlington, MA 01805.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

to achieve adequate pressures in the coronary sinus and excellent myocardial protection using retrograde cardioplegia alone.

References

1. Drinkwater DC, Laks H, Buckberg GD. A new simplified method of optimizing cardioplegic delivery without right heart isolation: antegrade/retrograde blood cardioplegia. J Thorac Cardiovasc Surg 1990;100:56–64.
2. Tomlinson DL, Goto H, Graf JC, Arakawa K. Incidental discovery of persistent left superior vena cava during cardiac surgery. Anesth Analg 1989;69:393–95.
3. Balasundaram S, Al-Halees Z, Duran CG. Persistent left superior vena cava: a simple technique for adequate drainage during cardiopulmonary bypass. J Cardiovasc Surg 1991;32: 59–61.

Notice From the American Board of Thoracic Surgery

The part I (written) examination will be held at the Hilton Executive Conference Center, Dallas Fort Worth Airport, Dallas, TX, on February 13, 1994. The closing date for registration is August 1, 1993.

To be admissible for the part II (oral) examination, a candidate must have successfully completed the part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the board in force at the time the application is received.

Please address all communications to the American Board of Thoracic Surgery, One Rotary Center, Suite 803, Evanston, IL 60201.

Post-Atherectomy Coronary Artery Aneurysm

Amram J. Cohen, MD, Alan Banks, MD, Patrick Cambier, MD, and
Fred H. Edwards, MD

Department of Surgery and Department of Cardiovascular Diseases, Walter Reed Army Medical Center, Washington, DC, and
Department of Surgery, Uniformed Services of the Health Sciences, Bethesda, Maryland

A 52-year-old man underwent an uneventful directional atherectomy of the left anterior descending coronary artery. Four months after the procedure unstable angina developed and on angiogram an aneurysm of the left anterior descending coronary artery was noted. The patient underwent bypass of the left anterior descending coronary artery. An attempt to exclude the aneurysm resulted in hemodynamic compromise and was discontinued. Follow-up angiogram 2 months after operation showed the aneurysm to be smaller. The patient is doing well 6 months after operation.

(Ann Thorac Surg 1992;54:1216–8)

Directional coronary atherectomy is a new, percutaneous interventional technique that mechanically removes atheromatous material. The complication rate and restenosis rate appear to be comparable with those of percutaneous transluminal coronary angioplasty [1]. An expanding role for the use of this intervention is expected [1]. Because resection depth is difficult to control, substantial disruption of the arterial media and adventitia, in up to 30% [2] of patients, has been described. Such an occurrence could theoretically predispose to aneurysm formation [2].

The patient is a 52-year-old man with no prior cardiac history. He experienced new-onset exertional angina culminating in a prolonged episode of chest pain. The diagnosis of a completed anteroseptal myocardial infarctation was made. Angiography demonstrated a high-grade complex coronary stenosis involving the left anterior descending coronary artery (LAD) (Fig 1). Thallium 201 stress testing was consistent with anterior reversible ischemia.

The patient was transferred to our institution, and directional coronary atherectomy was carried out using GFA Simpson Atherocath (Devices for Vascular Intervention, Redwood City, CA). Ten percent residual stenosis in the LAD was evident by angiography. There was no evidence of myocardial infarction. The patient was discharged within 48 hours.

Four months after atherectomy recurrent chest pain developed. Thallium 201 exercise testing revealed a perfusion abnormality in the distribution of the LAD, and angiography was repeated. Sequential obstructive stenoses were noted in the proximal LAD and first diagonal artery. A coronary aneurysm was present. The aneurysm measured 4.2 × 6 mm by comparison with the angiography catheter (Fig 2). The aneurysm encompassed the origin of the septal perforator and first diagonal artery. Despite maximal medical management, crescendo angina developed and the patient was referred for surgical revascularization.

The patient underwent cardiopulmonary bypass with moderate hypothermia and cold potassium cardioplegia. The aneurysm was exposed and excluded from the circulation by placement of ligatures proximal, distal, and posterior to the aneurysm. The aneurysm appeared firm and thick-walled with no evidence of imminent rupture (Fig 3). A left internal mammary artery graft was constructed distal to the aneurysm, and a reverse saphenous vein graft was placed proximal to the aneurysm. The patient could not be weaned from bypass, and transesophageal echocardiography demonstrated severe anterior and septal hypokinesis of the left ventricle. A second reverse saphenous vein graft was placed to the distal LAD. This did not improve the hemodynamic situation. The ligatures were removed from around the aneurysm, and septal motion improved such that the patient could be weaned from cardiopulmonary bypass. He was discharged after a 2-week hospital course.

He returned for follow-up 2 months after the procedure. Exercise stress testing showed no evidence of ischemia. Angiography demonstrated the grafts distal to the aneurysm to be patent. The vein graft permitted visualization of LAD and aneurysm (Fig 4). The aneurysm measured 3.2 × 3.8 mm. The patient is currently doing well 6 months after operation.

Comment

The presence of post-atherectomy coronary aneurysms (PACAs) raises two important questions. First, is the presence of such an aneurysm an indication for operation? Second, if the patient needs surgical revascularization for other reasons, how should the aneurysm be managed intraoperatively?

Atherosclerotic coronary aneurysms have been well studied. Clearly the presence of such an aneurysm is not

---

Accepted for publication March 18, 1992.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Address reprint requests to Dr Edwards, Cardiothoracic Surgery, Walter Reed Army Medical Center, Washington, DC 20307-5001.

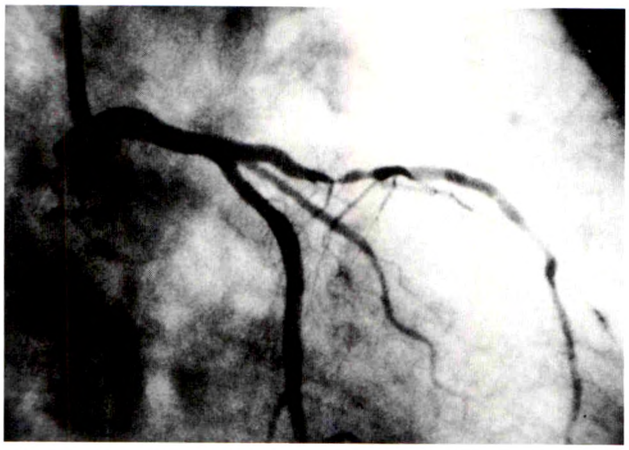


Fig 1. Right anterior oblique projection of a complex LAD lesion.

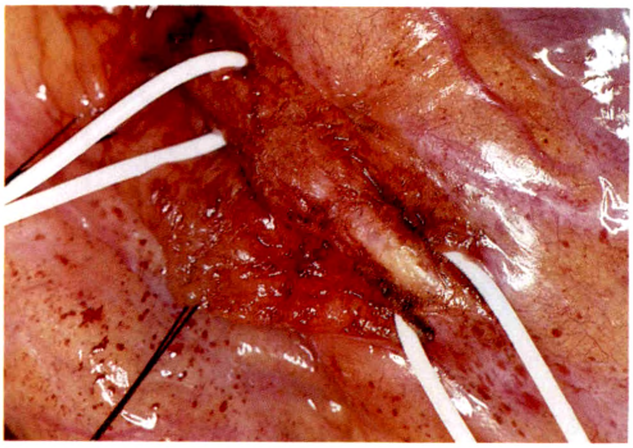


Fig 3. Intraoperative photo of mobilized LAD aneurysm.

an indication for operation. Early reports suggested that at the time of coronary artery bypass grafting, atherosclerotic coronary aneurysms should be excluded from the circulation to prevent rupture or embolization [3]. Subsequent larger series note no evidence of aneurysm rupture and no increased evidence of myocardial infarction in the coronary system with the aneurysm. The authors of these series do not advocate surgical treatment directed at the aneurysm at the time of coronary artery bypass grafting [4, 5].

Atherosclerotic aneurysms, however, are true aneurysms, whereas inadvertent resection of media or adventitia should cause a false aneurysm. Such aneurysms in other locations expand, rupture, and are an indication for operation [6, 7]. This case suggests that PACAs may behave like true aneurysms. The aneurysm at operation was thick-walled and did not appear prone to rupture. Despite undergoing surgical dissection and being left in the coronary circulation, the aneurysm did not expand over 2 months of follow-up.

Finally, proximal LAD lesions are the most common undergoing atherectomy [1]. Thus, PACAs may commonly occur at the site seen in our patient. Exclusion of such an aneurysm will require the sacrifice of important septal perforating branches. The acute sacrifice of such septal perforators without good collateral circulation has been shown to be a major cause for morbidity in other cardiac procedures and was probably the cause of hemodynamic instability in our patient. Thus, exclusion of PACAs in the proximal LAD system may be associated with serious morbidity with no clear benefit.

Our case suggests that PACAs do not necessarily expand rapidly and rupture and do not represent an indication for operation without evidence of rapid expansion or embolization. Sacrifice of septal perforators in the LAD system to exclude PACAs at the time of operation may cause serious hemodynamic instability and is not warranted. The intraoperative management of PACAs in the circumflex and right coronary system and the use of anticoagulants to prevent embolization remain open questions.

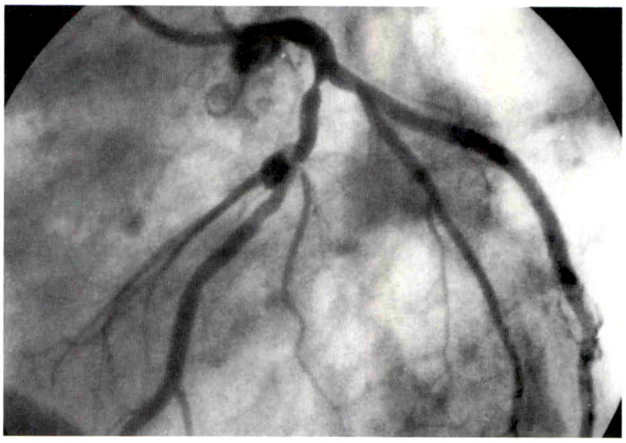


Fig 2. Left anterior oblique projection demonstrating obstructive LAD lesion associated with a coronary artery aneurysm.

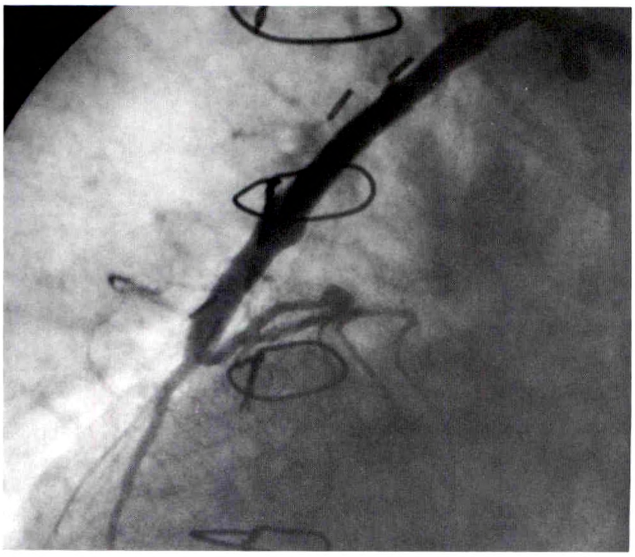


Fig 4. Left anterior oblique projection. The proximal LAD is visualized via retrograde flow through a distal vein graft. The aneurysm appears smaller.

Addendum

We have recently treated a second patient in whom a PACA developed in the proximal LAD. The patient was treated with coronary artery bypass grafting without exclusion of the aneurysm and is doing well 2 months after operation.

References

1. Robertson GC, Hinohara T, Selmon MR, Johnson DE, Simpson JB. Directional coronary atherectomy. Inter Cardio 1990: 563–78.
2. Garratt KN, Kaufman UP, Edwards WD, Vlietstra RE, Holmes DR. Safety and percutaneous coronary atherectomy with deep arterial resection. Am J Cardiol 1989;64:538–40.
3. Anabtawi IN, deLeon JA. Arteriosclerosis aneurysms of the coronary arteries. J Thorac Cardiovasc Surg 1974;68:226–8.
4. Robinson FC. Aneurysms of the coronary arteries. Am Heart J 1985;109:129–34.
5. Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients. Br Heart J 1985;54:392–5.
6. Vlodaver Z, Coe JI, Edwards JE. True and false left ventricular aneurysms: propensity for the latter to rupture. Circulation 1975;51:567–72.
7. Auella RJ, Hankins JR, Turney SZ, Cowley RA. Ruptured thoracic aorta due to blunt trauma. J Trauma 1977;17:199–205.

Giant Intrapericardial Solitary Fibrous Tumor

Uberto Bortolotti, MD, Francesco Calabrò, MD, Monica Loy, MD, Giuseppe Fasoli, MD, Giuseppe Altavilla, MD, and Domenico Marchese, MD

Departments of Cardiovascular Surgery, Thoracic Surgery, Cardiology, and Pathology, University of Padova Medical School, Padova, Italy, and Servizio di Cardiologia, Ospedale Civile di Piove di Sacco, Italy

A 60-year-old man with a large pericardial effusion was found to have a giant intrapericardial solitary fibrous mesothelioma firmly attached to the ascending aorta and pulmonary trunk. Nine months after excision of the mass the patient is free from symptoms and signs of tumor recurrence. Solitary fibrous mesothelioma is a rare benign tumor and its excision is curative; however, because of the lack of information on its long-term behavior, close noninvasive follow-up of this patient is necessary.

(Ann Thorac Surg 1992;54:1219–20)

Solitary fibrous mesotheliomas are rare tumors that most frequently arise from the pleura [1–3]. Their location within the pericardial sac, as in the case herein described, is exceedingly rare.

A 60-year-old man was occasionally found to have moderate cardiomegaly in 1989. In January 1991 he required hospitalization because of fatigue, anemia, chest discomfort, and increasing dyspnea of recent onset. On admission pulse rate was 104 beats/min and blood pressure was 170/100 mm Hg. Jugular venous distention and mild peripheral edema were present. The heart sounds were distant with no murmurs and the liver was palpable 2 cm below the costal border. The electrocardiogram showed sinus tachycardia with complexes of reduced amplitude and nonspecific ST changes, and a chest roentgenogram revealed marked cardiomegaly. A two-dimensional transthoracic echocardiogram showed the presence of abundant pericardial effusion, normal ventricular function, and a large intrapericardial mass anterior to the right ventricle (Fig 1A). Pericardiocentesis yielded approximately 900 mL of serohematic fluid with absence of neoplastic cells. Computed tomography of the chest confirmed that the mass was located within the pericardium anterior to the ascending aorta and pulmonary trunk (Fig 1B).

The patient underwent operation on March 14, 1991. The chest was entered through a median sternotomy. After the pericardium was opened, a pear-shaped whitish mass was found firmly attached by means of a wide base of implantation to the anterior aspect of the ascending aorta and pulmonary trunk (Fig 2). With cardiopulmonary bypass on standby, by careful dissection the mass was excised with a large cuff of aortic adventitia. Meticulous hemostasis was required because of highly vascularized adhesions to the wall of both great vessels.

The tumor measured approximately 14 × 7 cm and weighed 270 g. Section showed a white tissue with whorled appearance and scattered hemorrhages. At histologic examination cellular areas were rich in fusiform

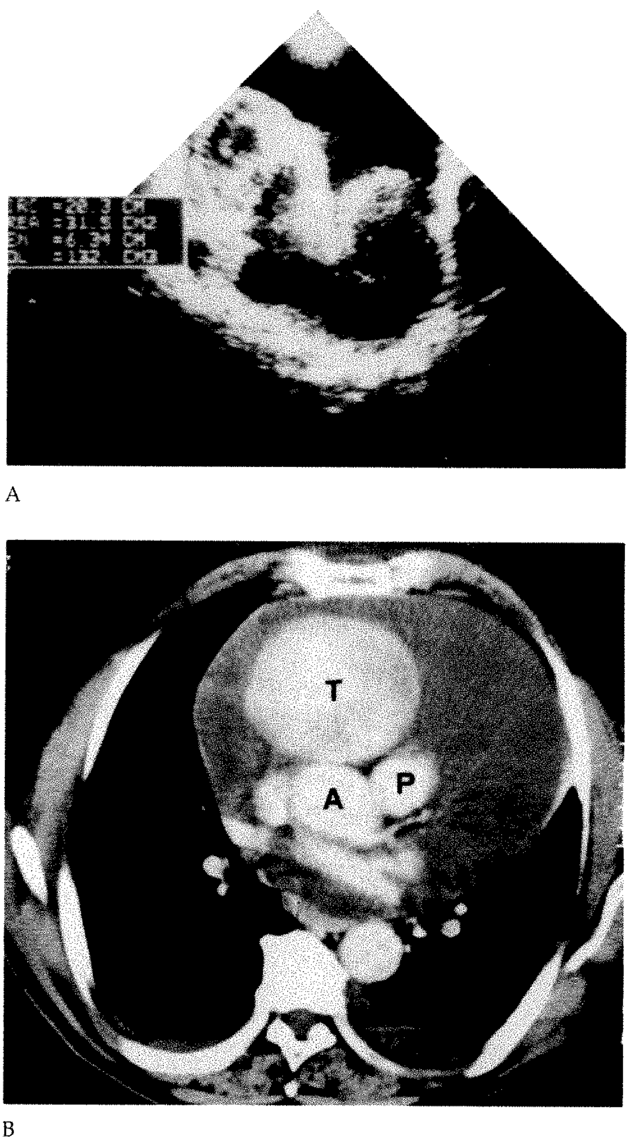


Fig 1. *(A) Transthoracic two-dimensional echocardiogram showing abundant pericardial effusion and the presence of an intrapericardial mass* (circled area) *anterior to the right ventricle. (B) Computed tomographic scan at the level of the origin of the great vessels. The presence of pericardial effusion and a large anterior intrapericardial tumor* (T) *in contact with both the ascending aorta* (A) *and pulmonary trunk* (P) *is confirmed.*

Accepted for publication March 19, 1992.

Address reprint requests to Dr Bortolotti, Istituto di Chirurgia Cardiovascolare, Centro di Cardiochirurgia "V. Gallucci," Via Giustiniani, 2, 35128 Padova, Italy.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

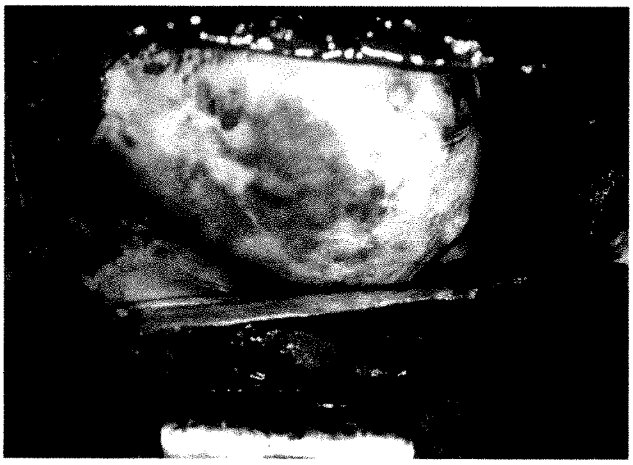


Fig 2. Intraoperative view, after opening of the pericardium, of the mass, which almost completely covers the anterior surface of the heart. The patient's head is on the left.

fibroblastlike cells at times arranged in bundles, whereas in other areas collagen fibers predominated with few cells; no mitoses were observed (Fig 3). At electron microscopy tumor cells showed fusiform central nuclei, and the cytoplasm contained few organelles and bundles of microfilaments. Immunohistochemical study showed diffuse reactivity to vimentin and negative staining for keratin.

The patient recovered uneventfully and is asymptomatic 9 months after operation. A two-dimensional echocardiogram and computed tomography of the chest showed absence of pericardial effusion and no signs of tumor recurrence.

Comment

Solitary fibrous tumors, or the so-called localized fibrous mesotheliomas, are well-known neoplasms of the serosal cavities that were first recognized as a distinct entity by Klemperer and Rabin in 1931 [4]. The vast majority of these tumors arise from the pleura [1–3], and their growth into the pericardium is extremely uncommon. In reviewing the literature we have found only 2 cases of intrapericardial mesothelioma. El-Naggar and associates [5], reporting in 1989 14 patients with localized fibrous tumors of the serosal cavities, described a patient with a large pericardial mass that was surgically excised; local recurrence was observed after 120 months with no further recurrence after reoperation. Roggli and co-workers [6], in their review on the pathology of human mesothelioma, showed a figure of another such case without giving clinical details.

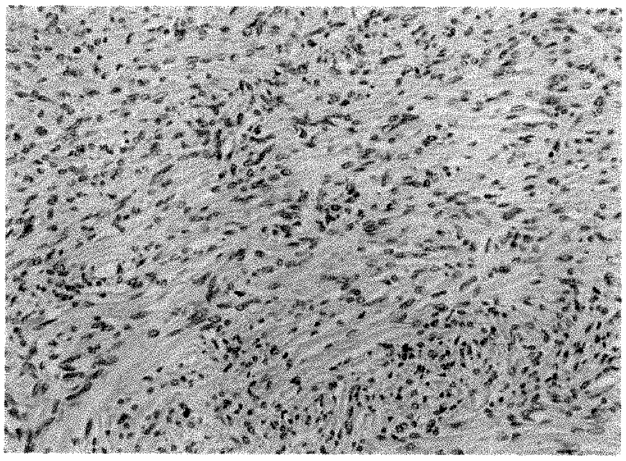


Fig 3. Histologic section of the mass (solitary fibrous mesothelioma) showing moderate cellularity consisting of fibroblastlike cells in less collagen matrix. (Hematoxylin and eosin; ×160 before 26% reduction.)

Although controversy still exists on the histogenesis of this neoplasm, immunohistochemical and ultrastructural studies have suggested that it most likely originates from pluripotential mesenchymal cells located in the subserosal connective tissue [5, 7, 8].

Localized mesotheliomas are considered to be benign neoplasms, and their excision is curative in most cases [2, 5]. However, in up to 12% of cases the tumor may be responsible for death because of its extensive intrathoracic growth, unresectable recurrences, or metastatic diffusion [1, 2].

The patient herein described had a giant intrapericardial solitary fibrous mesothelioma that was successfully excised. Solitary fibrous mesotheliomas of the pericardium are exceptionally rare tumors, and due to the lack of experience with such neoplasms and their often unpredictable behavior long-term prognosis in this patient remains uncertain. Even if radical excision has been obtained and no signs or regrowth are evident after 9 months, continuous noninvasive follow-up is mandatory because tumor recurrence also has been observed in the rare intrapericardial location [5].

References

1. Dalton WT, Zolliker AS, McCaughey WTF, Jacques J, Kannerstein M. Localized primary tumors of the pleura. An analysis of 40 cases. Cancer 1979;44:1465–75.
2. Briselli M, Mark EJ, Dickersin GR. Solitary fibrous tumors of the pleura: eight new cases and review of 360 cases in the literature. Cancer 1981;47:2678–89.
3. England DM, Hochholzer L, McCarthy MJ. Localized benign and malignant fibrous tumors of the pleura. A clinicopathological review of 223 cases. Am J Surg Pathol 1989;13:640–58.
4. Klemperer P, Rabin CB. Primary neoplasms of the pleura: a report of five cases. Arch Pathol 1931;11:385–412.
5. El-Naggar AK, Ro JY, Ayala AG, Ward R, Ordonez NG. Localized fibrous tumor of the serosal cavities. Immunohistochemical, electron-microscopic, and flow-cytometric DNA study. Am J Clin Pathol 1989;92:561–5.
6. Roggli VL, Kolbeck J, Sanfilippo F, Shelburne JD. Pathology of human mesothelioma. Etiologic and diagnostic considerations. In: Rosen PP, Fechner RE, eds. Pathology annual, part 2, Vol 22. Norwalk/San Mateo: Appleton & Lange, 1987:91.
7. Dervan PA, Tobin B, O'Connor MO. Solitary (localized) fibrous mesothelioma: evidence against mesothelial cell origin. Histopathology 1986;10:867–75.
8. Steinetz C, Clarke R, Jacobs GH, Abdul-Karim FW, Petrelli M, Tomashefski JF Jr. Localized fibrous tumor of the pleura: correlation of histopathological, immunohistochemical and ultrastructural features. Pathol Res Pract 1990;186:344–57.

Management of Severe Bronchial Ischemia After Bilateral Sequential Lung Transplantation

Derya Oturanlar, MD, Walter Klepetko, MD, Michael Grimm, MD, Adelheid End, MD, Wilfried Wisser, MD, Thomas Wekerle, MD, and Ernst Wolner, MD

Second Surgical Department University of Vienna, Vienna, Austria

A case of severe diffuse bronchial ischemia after bilateral sequential lung transplantation is presented. A combination of initial conservative treatment with silicone stenting and late bilateral retransplantation under stable conditions resulted in good clinical outcome. Factors in decision making and technical aspects of the stenting procedure are discussed.

(Ann Thorac Surg 1992;54:1221–2)

Although bronchial anastomotic complications after lung transplantation have been frequently described in the past [1], complete bronchial ischemia remains a rare event. If early bronchial dehiscence [2] does not occur, the usual result is severe instability and malacia of the bronchial system, which later on is followed by heavy shrinking and late scar formation.

A 38-year-old man underwent bilateral sequential lung transplantation for treatment of end-stage emphysema. Preservation of the lungs was performed by pulmonary artery flushing with 60 mL/kg of cold modified Euro-Collins solution. Ischemic time for the lungs was 300 and 394 minutes, respectively. Both anastomoses were performed using a telescope technique with interrupted 3-0 PDS (Ethicon, Germany) sutures and were wrapped with intercostal muscle flaps. Intraoperative bronchoscopy showed normal anastomoses and distal bronchial mucosa. Immunosuppression consisted of 1 g of methylprednisolone intraoperatively, followed by a regimen of cyclosporin A, azathioprine, and antithymocyte globulin for 7 days. Prednisolone was administered starting with the 14th postoperative day. The initial postoperative course was uneventful. The patient had excellent gas exchange, was extubated 32 hours after the procedure, and was transfered to the normal ward on the 5th postoperative day.

On the 7th postoperative day increasing mucous production at coughing was noticed. By the 10th postoperative day the patient complained about increasing dyspnea, which made reintubation necessary. At bronchoscopy, severe bilateral ischemia of the donor bronchus, extending from the level of the anastomosis (Fig 1) down to the lower lobe segmental orifices (Fig 2), was observed. Because the patient had no signs of bronchial dehiscence, conservative treatment with mechanically assisted ventilation was initiated. Three weeks later, the patient experienced spontaneous perforation of a duodenal ulcer. The ulcer was excised and oversewn, and selective proximal vagotomy was performed. At the end of the procedure bronchoscopy was performed. Still ischemic bronchial wall was visualized and a first attempt to stent both main bronchi with two 10-mm silicone stents was made. With these devices, weaning from ventilatory support was possible within few days. However, the patient still frequently required bronchoscopic suction to clear his enormous mucous secretions. In addition, it became obvious that stenting of the main bronchi was not sufficient to overcome the problem of bronchomalacia in the region of the lobar bronchi.

After several attempts with different stents, complete stenting of the upper-lower lobe carina and the lobar bronchi was finally achieved by the insertion of small silicone T tubes (7 mm diameter) with their ends cut to a length to extend into the lobar bronchi down to the level of the segmental orifices (Fig 3). These stents were placed through a rigid bronchoscope, and final positioning was performed with a rigid forceps. The patient's respiratory function improved impressively, and 84 days after the initial transplantation he was discharged from the hospital with satisfactory lung function (vital capacity 79% of predicted, forced expiratory volume in the first second 64% of predicted).

One hundred sixty-three days after the transplantation he was readmitted to the hospital with sudden severe dyspnea due to stent dislocation. Repositioning of the stents was not possible, and when a suitable donor became available, bilateral sequential retransplantation through two separate thoracotomies was performed on the same day. The following postoperative course was uneventful, and the patient was discharged 22 days after the repeat transplantation. He remains in excellent clinical condition with normal lung function 1 year later.

Pathological examination of the lungs revealed severe bronchomalacia of the central parts of the bronchi together with more distal localized poststenotic bronchiectasis and focal pneumonic infiltrates. No evidence of bronchiolitis or chronic rejection was found.

Comment

Interruption of the bronchial nutritive circulation is known to be the major reason for impaired blood supply to the bronchial tree after lung transplantation [3]. Nor-

---

Accepted for publication March 20, 1992.

Address reprint requests to Dr Klepetko, Second Surgical Department, University of Vienna, Spitalgasse 23, A-1090 Vienna, Austria.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

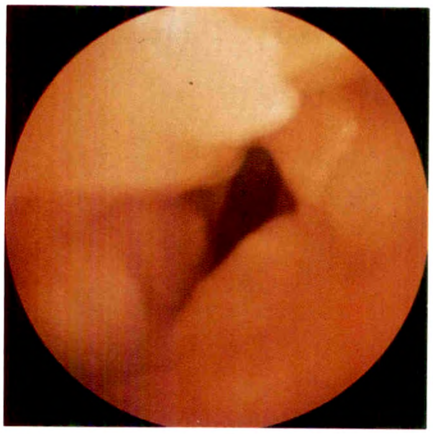


Fig 1. Bronchoscopic view on the 10th postoperative day. Beginning at the level of the bronchial anastomosis the bronchial mucosa appears completely ischemic.

mally, revascularization is soon achieved by intrapulmonary collaterals deriving from the pulmonary arterial system, and microcirculation plays a major role in restoration of nutritive blood supply [4]. Alternative techniques of early bronchial revascularization are omental wrapping or direct bronchial revascularization.

In the patient described here, the exact reason for the complete bronchial ischemia must remain speculative. Ischemic time of the lungs did not exceed 7 hours, a period for which satisfying graft function has been observed in at least 30 other lung transplants at our institution. In addition, dissection of the bronchial tree was avoided as far as possible.

Once bronchial problems after lung transplantation occur, their effective management is crucial to achieve good long-term outcome. By far most disturbances in bronchial healing occur at the site of the bronchial anastomosis and result in a localized stenosis [1, 5]. Management of these circumscript problems with endoluminal silicone stenting has been described. In contrast, the presence of complete bronchial ischemia extending over a distance of several centimeters results in complex damage to the bronchial tree with consequent necrosis of the mucosa and underlying structures and collapse of the bronchial wall. Extensive scar formation and bronchomalacia are the late sequelae, which most likely can only be treated by retransplantation. However, performing a retransplantation in the early postoperative period has a much higher risk than late repeat transplantation under stable conditions, and we therefore decided to treat our patient conservatively in the initial phase. Because initial stenting 10 days after the transplantation seemed to have a high risk for disruption of the anastomoses, the patient underwent temporary tracheostomy and mechanical ventilatory support. Three weeks later, stenting was performed at a time when healing of the bronchial anastomoses was expected to be sufficient.

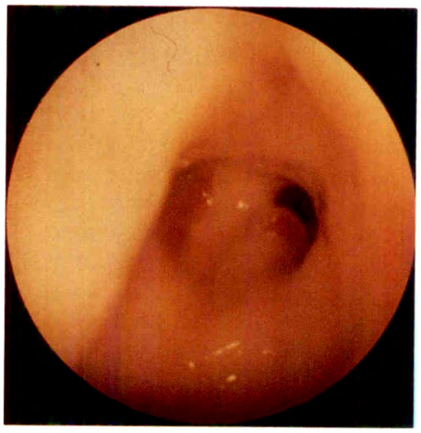


Fig 2. A more distal bronchoscopic view shows the beginning of mucosa supplied with blood at the level of the lower lobe segmental orifices.

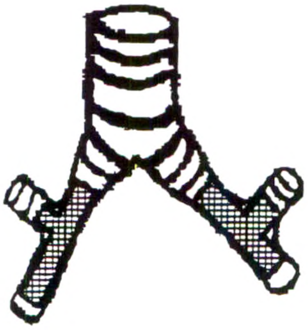


Fig 3. Schematic drawing of the stented bronchial area.

The use of small silicone T tubes for stenting of the lobar carina and lobar bronchi represented a new approach to the problem of extensive distal airway stenosis [1]. The functional result of this procedure was surprisingly good and allowed complete rehabilitation of the patient. We have since used this approach with good results in other patients in whom a bronchial anastomotic stenosis closed to the upper lobe orifice was present.

References

1. Schaefers HJ, Haydock DA, Cooper JD. The prevalence and management of bronchial anastomotic complications in lung transplantation. J Thorac Cardiovasc Surg 1991;101:1044–52.
2. Kirk AJB, Conacher ID, Corris PA, Ashcroft T, Dark JH. Successful surgical management of bronchial dehiscence after single-lung transplantation. Ann Thorac Surg 1990;49:147–9.
3. LoCicero J, Massad M, Matano J, Greene R, Dunn M, Michaelis LL. Contribution of the bronchial circulation to lung preservation. J Thorac Cardiovasc Surg 1991;101:807–15.
4. Turrentine MW, Kesler KA, Wright CD, et al. Effect of omental, intercostal, and internal mammary artery pedicle wraps on bronchial healing. Ann Thorac Surg 1990;49:574–9.
5. Maurer JR, Morrison D, Winton TL, Patterson GA. Late pulmonary complications of isolated lung transplantation. Transplant Proc 1991;23:1224–5.

Permanent Pacemaker Implantation in Premature Infants Less Than 2,000 Grams of Body Weight

Mikio Ohmi, MD, Motohisa Tofukuji, MD, Kaori Sato, MD, Takahiko Nakame, MD, Naoshi Sato, MD, Kiyoshi Haneda, MD, and Hitoshi Mohri, MD

Department of Thoracic and Cardiovascular Surgery, Tohoku University School of Medicine, Sendai, Japan

Pacemaker implantation in premature infants presents technical problems because of the relatively larger size of the pulse generator compared with their bodies. A new technique with which successful generator implantation was performed in 2 premature infants less than 2,000 g of body weight is described. The generator is wrapped in a Gore-Tex surgical membrane. A piece of membrane overlying the electrical contact surface of the generator is removed, and the generator is fixed to the abdominal wall in the peritoneal cavity. The technique is simple to perform and would give relative ease in generator exchange.

(Ann Thorac Surg 1992;54:1223–5)

Recent advancement in pacemaker technology has expanded the indications for pediatric cardiac pacing. Small pulse generators have been available for clinical use, and many surgical techniques for generator placement have been introduced [1–7]. However, the placement of a relatively large generator compared with the size of a premature infant is associated with many technical problems and remains a source of many complications. In this article, a new technique of pacemaker implantation in a peritoneal cavity that is simple to perform and easily applied to premature infants weighing less than 2,000 g is described.

Patients

Two female patients with congenital atrioventricular block diagnosed by fetal echocardiography were delivered by cesarean section. Both patients showed positive circulating maternal syndrome Sjögren A antibody, and 1 patient's condition was complicated with hydrops fetalis. Their birth weights were 1,680 and 1,840 g with estimated gestational ages of 33 and 29 weeks and heart rates at birth of 55 and 48 beats/min, respectively. They were placed on bradycardia treatment with emergency temporary pacing in the delivery room.

One patient received a transvenous pacing lead from the femoral vein by means of cutdown, and the lead was advanced to the right ventricle under fluoroscopic control. After 5 days of temporary pacing, pacing failure occurred because of right ventricular perforation by the pacing lead tip. Emergency permanent pacemaker implantation was performed using a myocardial lead through a left anterolateral thoracotomy, and a pulse generator was implanted in the subcutaneous layer of the left abdomen. The skin over the generator was markedly protruded and turned reddish a few days later. Fluid accumulation was detected in the generator pocket. To prevent skin necrosis, we relocated the generator in a pocket of the peritoneal cavity when the patient was 14 days old.

The other patient received two temporary epicardial leads on the right ventricle through a median sternotomy in the delivery room followed by elective pacemaker implantation in the peritoneal cavity at 20 days of life.

Technique

A small left anterolateral thoracotomy through fourth or fifth intercostal space is performed and the pericardium is opened. The myocardial lead (model 325-452; TPL-Cordis, Inc, Englewood, CO) is attached to the epicardium of the left ventricle. After laparotomy is made using a midline abdominal incision, the lead is introduced from the left pleural cavity to the subcutaneous layer of the left upper abdomen, where the lead is looped. The lead then is passed through the abdominal muscle layer and peritoneum into the peritoneal cavity and connected to the generator (Nova II, model 281-05S; Intermedics, Inc, Freeport, TX). The generator is wrapped in a sheet of Gore-Tex surgical membrane (W.L. Gore & Associates, Inc, Flagstaff, AZ). This membrane pocket is secured around the generator using silk sutures placed in the periphery of the folded membrane. A round piece of membrane overlying the electrical contact surface of the generator is removed (Fig 1). Several sutures that have been placed in the folded membrane are sutured to the abdominal wall in the peritoneal cavity with the electrical contact surface of the generator turned anteriorly toward the peritoneum (Fig 2). With the pacemaker implanted and functional, the midline incision is closed. The anteroposterior roentgenogram taken 1 month after the implantation is demonstrated in Figure 3.

The postoperative course of the 2 patients was uneventful. The generator did not migrate and its position could be confirmed by palpation through the abdominal wall.

Accepted for publication July 13, 1992.

Address reprint requests to Dr Ohmi, Department of Thoracic and Cardiovascular Surgery, Tohoku University School of Medicine, 1-1 Seiryo-cho, Aoba-Ku, Sendai, 980, Japan.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

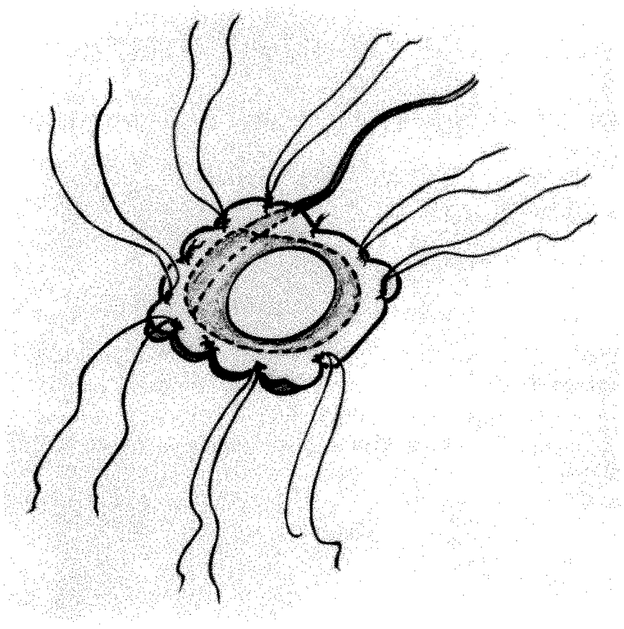


Fig 1. The pulse generator is wrapped in a sheet of Gore-Tex surgical membrane with suspension sutures. A round piece of membrane overlying the electrical contact surface of the generator is removed.

Comment

Complete atrioventricular block is an uncommon congenital disease, occurring in about 1 of 20,000 newborns. Recent advances in fetal echocardiography facilitate early diagnosis of the presence and nature of diseases. Because one of the most common causes of the disease is maternal connective tissue diseases, which may progress against a rational therapeutic regimen, it is important to assess which fetus requires therapy. Hydrops fetalis, as in one of our patients, and fetal or neonatal death appear to be associated with ventricular rates less than 55 beats/min [8]; we therefore elected to deliver our patients prematurely and begin treatment with pacemaking.

Although there have been several reports on pacemaker implantation in infants and young children, few have been published on premature infants. Various implantation sites have been employed to avoid the problems of patient discomfort, skin bulge, skin necrosis with infection, generator migration, and technical difficulties during generator exchange. Subcutaneous implantation is common for adult patients because of the simplicity of implanting and replacing the generator; however, the scanty subcutaneous fat, thin skin, and exposed position of the generator stretching the skin over the generator invite skin necrosis and infection in small infants. Retroperitoneal, intrapelvic, and intrapleural generator placements provide the possibility of generator migration and interference with major organs contained therein and result in technical problems when the generator requires exchange.

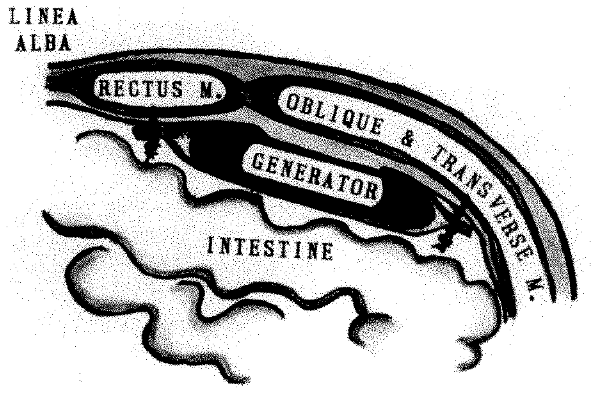


Fig 2. The pulse generator wrapped in a Gore-Tex membrane blanket is attached to the peritoneum with the electrical contact surface of the generator turned anteriorly toward to the peritoneum.

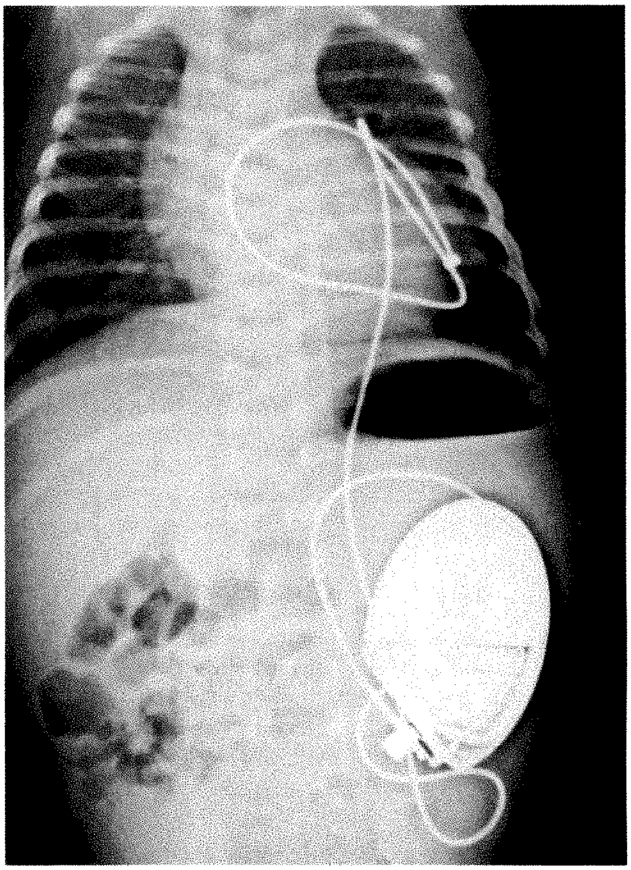


Fig 3. Anteroposterior roentgenogram shows the large pacemaker generator in the peritoneal cavity. The lead is looped in the pericardial and pleural cavities and the subcutaneous layer of the left abdomen.

Subrectal, intermuscular, and preperitoneal placement or preperitoneal placement with suspension by the anterior abdominal fascia might be acceptable for infants; however, the peritoneum, fascia, and muscle of premature infants are too thin and fragile to create a relatively large generator pocket. Our technique of intraperitoneal generator placement using a Gore-Tex surgical membrane pocket provides maximal space to implant the generator and reliable fixation to prevent generator migration. Furthermore, the generator can be exchanged without opening into the free peritoneal cavity because the generator is in the pocket and attached to the peritoneum.

References

1. Idriss FS, Otto R, Nikaidoh H, Newfeld E, Paul MH. Implantation of permanent pacemaker in the first month of life for congenital complete heart block. J Thorac Cardiovasc Surg 1973;65:851–5.
2. Salama FD. A suggested site for the implantation of myocardial pacemakers in infants and young children. Thorax 1976; 31:346–9.
3. Donahoo JS, Haller JA, Zonnebelt S, Neil C, Gott VL, Brawley RK. Permanent cardiac pacemakers in children: technical considerations. Ann Thorac Surg 1976;22:584–7.
4. Amato JJ, Payne DD, Rheinlander HF, Cleveland RJ. Intermuscular abdominal implantation of permanent pacemakers in infants and children. Ann Thorac Surg 1978;25:243–7.
5. Culliford AT, Isom OW, Doyle E. Pacemaker implantation in the extremely young. A safe and cosmetic approach. J Thorac Cardiovasc Surg 1978;75:763–4.
6. DeLeon SY, Ilbawi MN, Idriss FS. Pacemaker implantation in infants and children: a simplified approach. Ann Thorac Surg 1980;30:599–601.
7. Robertson JM, Laks H. A new technique for permanent pacemaker implantation in infants and children. Ann Thorac Surg 1987;44:209–11.
8. Schmidt KG, Ulmer HE, Silverman NH, Kleinman CS, Copel JA. Perinatal outcome of fetal complete atrioventricular block: a multicenter experience. J Am Coll Cardiol 1991;91:1360–6.

Replacement of Paracorporeal Ventricular Assist Devices

Douglas P. Lohmann, ME, Lawrence R. McBride, MD, D. Glenn Pennington, MD, and Marc T. Swartz, BA

Department of Surgery, St. Louis University Medical Center, St. Louis, Missouri

In this communication we describe a technique to change paracorporeal ventricular assist devices after the development of mechanical complications. This procedure is technically simple and in our experience does not require a sternotomy or cardiopulmonary bypass. Paracorporeal ventricular assist devices can be safely changed allowing continued support and survival.

(Ann Thorac Surg 1992;54:1226–7)

Between February 1988 and February 1992, 30 patients received investigational pulsatile ventricular assist devices (VADs) at St. Louis University. During this same period 4 patients required VAD replacement due to device-related problems. These patients had paracorporeal VADs of the Pierce-Donachy design [1] (Thoratec Laboratories Corp, Berkeley, CA, and Sarns/3M, Ann Arbor, MI). There were 3 men and 1 woman ranging in age from 28 to 54 years (mean, 44 years). Two patients required VAD insertion after development of acute myocardial infarction shock, and the condition of 2 patients with cardiomyopathy (idiopathic, 1, and postpartum, 1) deteriorated while they were awaiting cardiac transplantation. The duration of support ranged from 52 to 89 days (mean, 69 days).

The circumstances necessitating replacement of the VADs were varied and included severe hemolysis, a ruptured blood sac, destruction of the outer pump casing, and partial cannula obstruction. Ventricular assist device replacement occurred 6, 35, 45, and 79 days after insertion. Three of the 4 patients were ambulatory at the time of replacement. The first patient had severe hemolysis (serum hemoglobin level, 1.15 g/L) due to a previously unrecognized flaw in the design of the VAD valve housing clearances. The hemolysis was corrected within 12 hours by replacing the Sarns VAD with another more established VAD (Thoratec) of similar design. This man's heart recovered after 53 days of support, and he was weaned from the VAD and discharged from the hospital.

The second patient is a 28-year-old woman who had a ruptured blood sac. This tear was due to an error in the quality control procedures on the part of the manufacturer. On the 45th day after left VAD implantation a large thrombus appeared and was believed to be located within the blood sac. The thrombus did not interfere with VAD function and the patient remained in hemodynamically stable condition. After the VAD was removed, replaced, and disassembled the clot was found to be located between the blood sac and the rigid pump housing. Blood had leaked from the blood sac into this space through a small tear and clotted. During VAD replacement it appeared that native heart function had substantially improved; 9 days later the patient was weaned from the assist device and soon thereafter discharged.

The third patient was a 46-year-old man with biventricular assist devices who required replacement of both pumps when acetone destroyed the outer pump casings [2]. The acetone did not come in direct contact with the VADs but was used to remove tape residue from an area adjacent to the devices. Acetone vapors, even in trace amounts, can cause fractures in polysulfone plastics and therefore should not be used in the vicinity of these materials.

The last patient had decreasing flows (1.9 L/min) through his right VAD. This problem was presumed to be mechanical in nature; however, upon inspection of the removed right VAD, the valves were functioning properly with no obstructions and the Hall effect switch was operating correctly. A new VAD was connected, but there was no improvement in flow. The sternotomy was reopened and the right VAD removed. Because right heart function had recovered substantially only low-dose isoproterenol was necessary. It appeared that the lighthouse tip of the right atrial cannula had been intermittently and partially occluded by right atrial tissue. This man was successfully supported with the left VAD until a suitable donor heart was found; he was subsequently discharged after transplantation.

Technique

After the induction of general anesthesia, adequate intravenous lines are placed for drug delivery and volume replacement. An arterial line and a Swan-Ganz catheter are inserted; the patient is then anticoagulated with heparin (1 mg/kg). As the VAD to be replaced is not sterile, extreme diligence should be taken to ensure that the VAD and the cannulas are as clean as possible. To do this povidone-iodine solution is applied to all VAD surfaces, and the surfaces are wiped dry with sterile towels and then resprayed with povidone-iodine. All surfaces should still be considered contaminated, and separation of sterile

---

Accepted for publication July 28, 1992.

Address reprint requests to Mr Lohmann, Department of Surgery, St. Louis University Medical Center, 3635 Vista Ave at Grand Blvd, St. Louis, MO 63110.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

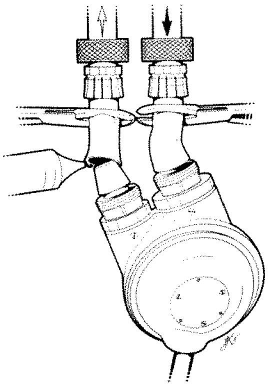


Fig 1. Removal of air from the replacement ventricular assist device.

and nonsterile fields should be maintained as much as possible. In addition, prophylactic antibiotics should be given to all patients undergoing this procedure. The VAD is halted and the cannulas are clamped. If necessary, administration of inotropic drugs is started to maintain adequate perfusion. If the heart is unable to support the circulation, VAD pumping should resume until cardiopulmonary bypass can be instituted. Femorofemoral cardiopulmonary bypass may be used to avoid reopening the sternal incision. With both the VAD inflow and outflow cannulas clamped, the old VAD is removed. The new VAD is then connected to the VAD inflow cannula. The VAD inflow cannula is slowly unclamped, allowing the blood sac to fill with blood. The VAD inflow cannula is reclamped. When the blood sac is nearly full of blood and evacuated of air, the VAD is partially connected to the VAD outflow cannula (Fig 1). Heparinized normal saline solution is then squirted on the connection while the outflow cannula and VAD are joined. The VAD is inspected to assure that all air is completely removed before the connections are tightened and VAD operation resumed.

Results

All of these patients received heparin during the exchange, and 3 received protamine at the end of the procedure. Two patients were receiving only dextran (25 mL/h) in the period before VAD replacement, and the remaining 2 were receiving a combination of warfarin (prothrombin time, 1.5 times control) and aspirin or warfarin and dipyridamole. There was no significant difference in the preoperative and postoperative activated partial thromboplastin time or prothrombin time. Transfusions averaged five units of packed red blood cells per patient. One patient required six units of packed red blood cells to replace blood lost before this procedure from a subclavian vein perforation. The patient who had his right VAD removed through a sternotomy received seven units of packed red blood cells in part to raise his right atrial pressure and increase left VAD output. We believe that patients without other complications should require little or no blood products. Inotropic drugs were necessary for a short period during the exchange in 3 patients; however, none of these patients required cardiopulmonary bypass. The exchange of pumps took less than 30 minutes in all cases. Two patients were extubated within 24 hours, 1 received a cardiac transplant 24 hours after VAD replacement, and the remaining patient was extubated 13 days later. All patients survived the procedure without complications. One patient died 54 days later of unrelated complications, and 3 were discharged. Of the 3 survivors 1 received a cardiac transplant and the other 2 were weaned from the VAD after cardiac recovery. As of June 1992 the 3 survivors are doing well (New York Heart Association functional class I) and have survived an average of 2 years after VAD removal.

Comment

Most of the circumstances that would require VAD replacement can be avoided by meticulous manufacturing quality control and care for these devices. However, should the necessity arise due to clinical needs, replacement remains a reasonable option. Although there are some limitations to this VAD design, the ability to replace it without much difficulty is encouraging. It is possible to exchange VADs without the need for cardiopulmonary bypass. Minimal additional anticoagulation is required to avoid thrombus formation during the brief period while the blood is stagnant in the cannulas. Inotropic drugs may be necessary for a short time (30 minutes) during the exchange of the VADs.

As the periods of VAD support increase, the amount of time that external VADs are exposed to potentially harmful environmental factors also increases. Some of those dangers have been identified in the ongoing clinical trials, such as our experience with acetone. As experience grows we can expect to see more complications such as those mentioned in this article. These devices were designed and tested for durations of support of less than 14 days. They certainly are versatile and have proved themselves capable of much longer periods of support (225 days, University of Pittsburgh; R. Kormos, personal communication, May 1992).

Only one of these complications could have been avoided by the use of an implantable VAD, the acetone incident. Blood sac perforation, cannula obstruction, and hemolysis could have just as easily occurred with an implantable pump; however, the resolution of the problem would have been considerably more difficult. As clinical experience grows, complications associated with these devices will continue to be identified. The ability to replace temporary paracorporeal pneumatic pumps without surgical intervention should be considered a noteworthy asset.

References

1. Donachy JH, Landis DL, Rosenburg G, Prophet GA, Ferrari O, Pierce WS. Design and evaluation of a left ventricular assist device: the angle port pump. In: Unger F, ed. Assisted circulation. Berlin: Springer-Verlag, 1979:138–46.
2. Lohmann DP, Pennington DG, McBride LR. Acetone: a hazard to plastic medical products—a case report [Letter]. J Thorac Cardiovasc Surg 1991;102:937–8.

Inverted Y Incision for Accurate Tailoring of Patches and Vessels

Darryl M. Hoffman, FRCS, and Robert W. M. Frater, FRCS

Department of Cardiothoracic Surgery, Albert Einstein College of Medicine, Bronx, New York

When anastomosing vessels or using a patch to close a defect, it is often difficult to trim the vessel end or patch to size once the anastomosis is underway. We describe an inverted Y technique that is easy, is completely reproducible, and provides for an even, accurate fit. A continuous suture is run from the heel along either side to the widest part of the anastomosis. A straight incision is made from the tip of the patch or toe of the vessel to a point corresponding to the apex of the defect to be filled; from this point, appropriately curved cuts are made to the edges of the patch or vessel just beyond the last sutures. The patch is now accurately shaped and the suture lines are completed.

(Ann Thorac Surg 1992;54:1228)

Anastomosing vessels and using a patch to close a defect are commonly performed procedures in cardiac and vascular surgery, and it is easy to have mismatch errors at the all-important toe portion of an anastomosis or patch plasty. A common difficulty is trimming a patch or vessel end to size after an anastomosis is already underway. This report describes a technique that is easy and completely reproducible. Ragged edges and the need for retailoring are avoided, and the method provides for an even, symmetrical, and accurate fit. The technique is applicable to patches for coarctation repair, right ventricular outflow tract or aortic root enlargement, or patch closures of all acquired or congenital cardiac defects and all end-to-side vascular anastomoses. Patches may be made oval or diamond-shaped as desired.

Shaping the tip of the vessel is clearly critical to ensuring optimal fit, hemostasis, and patency of an internal mammary artery anastomosis. After the anastomosis is commenced at the heel, sutures are run along each side to the point where the curve for the toe of the anastomosis should begin. Handling of the internal mammary artery is facilitated by opening the vessel 1 cm over and above the length needed for the anastomosis. By grasping the tip of the internal mammary artery that will be amputated, the surgeon may manipulate the internal mammary artery conveniently without compromising the principles of a no-touch technique [1].

Accurate tailoring is easily achieved by making a straight incision in the middle of the opened internal mammary artery from the tip to a point corresponding with the apex of the anastomosis (Fig 1A, *dotted line*). Now, appropriately curved cuts are conveniently made to the points where the last sutures were taken (Figs 1B, 1C). The suture line may be completed with either a continuous or multiple interrupted sutures according to the preference of the surgeon. Anastomosis of the internal mammary artery to a coronary vessel is used to illustrate the Y incision technique, but the method is equally useful for tailoring patches and other vessels.

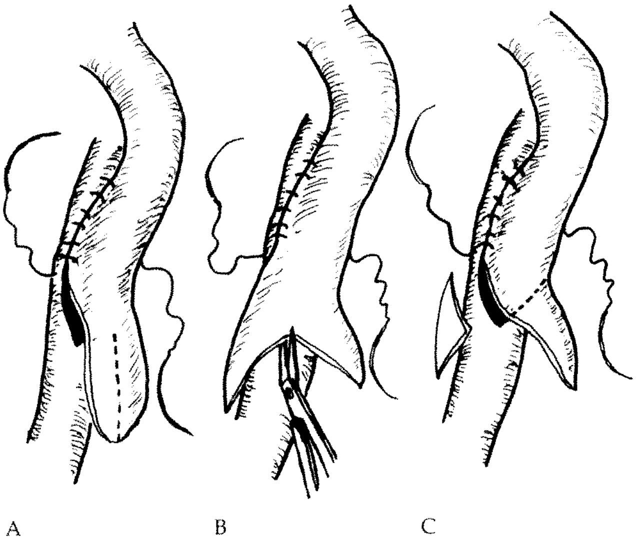


Fig 1. End-to-side anastomosis with the Y incision technique.

Reference

1. Galvin IF. Mammary artery grafts: a new no-touch technique for anastomosis. Ann Thorac Surg 1991;51:500–3.

Accepted for publication Aug 21, 1992.

Address reprint requests to Dr Hoffman, Department of Cardiothoracic Surgery, Allegheny General Hospital, 320 East North Ave, Pittsburgh, PA 15212.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Repairing the Degenerative Anterior Mitral Leaflet

John M. Alvarez, FRACS, Narcissus Teoh, MB, BS, and Cedric W. Deal, FRACS

Department of Cardiothoracic Surgery, Royal North Shore Hospital, Sydney, Australia

This is a consecutive, nonselected series of 18 patients with degenerative mitral regurgitation requiring a reparative operation on the anterior mitral leaflet. A new technique of double-breasting the two leaflets when flail septal segments are encountered is introduced.

(Ann Thorac Surg 1992;54:1229–30)

Eighteen consecutive patients with degenerative mitral regurgitation underwent operation on the anterior mitral leaflet. These patients belong to a series of more than 300 patients having mitral valve repairs at the Royal North Shore Hospital since 1970. By tailoring the repair to each patient, we have achieved successful repairs in more than 90% of patients with degenerative disease.

Material and Methods

There were 4 women and 14 men. The mean age was 61 years (range, 41 to 75 years). All patients had pure mitral regurgitation (MR); 7 were in New York Heart Association (NYHA) functional class III and 11 were in NYHA class IV preoperatively. All patients had preoperative cardiac ventriculography and two-dimensional echocardiography. The degree of MR was severe (MR jet fills the pulmonary veins) in 12 and moderate in 6 patients. The ejection fraction was less than 0.50 in 11 patients (range, 0.32 to 0.56; mean, 0.44).

We use antegrade blood cardioplegia with moderate hypothermia (28°C) for myocardial protection; the valve was exposed through a left atriotomy paralleling Sonnengaard's groove. Operative findings are shown in Table 1; all patients had more than four findings.

Having ascertained the cause of the MR, we tailored the repair to each factor by a combination of procedures (Table 2). When a flail septal segment of either leaflet was found and the leaflet in this area was not redundant, we sutured the margins of these leaflets together and reinforced this area with a posteromedial suture annuloplasty (Fig 1). When the flail septal segment was associated with redundant leaflet tissue in this area, we anchored the margins of the anterior mitral leaflet to the ventricular surface of the posterior leaflet and anchored the posterior leaflet onto the atrial surface of the anterior leaflet, ie, double-breasted the leaflets (see Fig 1). Again, this was reinforced with a posteromedial annuloplasty. Our standard method of repairing the posterior mitral leaflet [1] entails quadrangular excision of 60% to 70% of the posterior leaflet. Eight patients had coronary grafting. There were no deaths. All patients have had postoperative two-dimensional echocardiography, and since 1987 all have had transesophageal echocardiography. Follow-up is complete with a mean of 32 months (range, 2 to 102 months).

Results

Postoperatively 15 patients are in NYHA class I, and 3 are in NYHA class II (these were all in NYHA class IV preoperatively). Transesophageal echocardiography showed mitral valve surface areas of 3.3 ± 0.32 cm^2 for the entire series, 3.6 ± 0.32 cm^2 for patients with chordal transposition, 3.3 ± 0.57 cm^2 for those with double-breasting, and 3.2 ± 0.56 cm^2 for those having a septal commissuroplasty. Peak mitral valve gradients at rest were 1.3 ± 0.23 mm Hg for those with chordal transposition and 1.9 ± 0.37 mm Hg in both the commissuroplasty and the double-breasted groups. For the whole group the gradient was 1.6 ± 0.23 mm Hg.

Clinically 5 patients (28%) have a murmur, all grade 1. Echocardiography revealed MR in another 5 patients, a total of 55%. In 5 it is trivial (MR jet does not reach posterior atrial wall) and solely detected by transesophageal echocardiography, and in 5 it is mild (single jet reaches posterior atrial wall).

Comment

Repairing the mitral valve is clearly the goal of the surgeon. Although a degenerative etiology is ideally suited to this goal, the subset of patients with anterior mitral leaflet pathology is clearly a difficult group [2]. A

Table 1. Operative Findings

Finding	No. of Patients	Percent
Central cleft in AML	1	5.5
AML		
Flail central segment	8	45
Flail septal segment	12	66
PML: Flail central segment	15	82
Chordal rupture	12	66
Chordal elongation	12	66
Thickened leaflets	9	50
Annular dilatation	18	100

AML = anterior mitral leaflet; PML = posterior mitral leaflet.

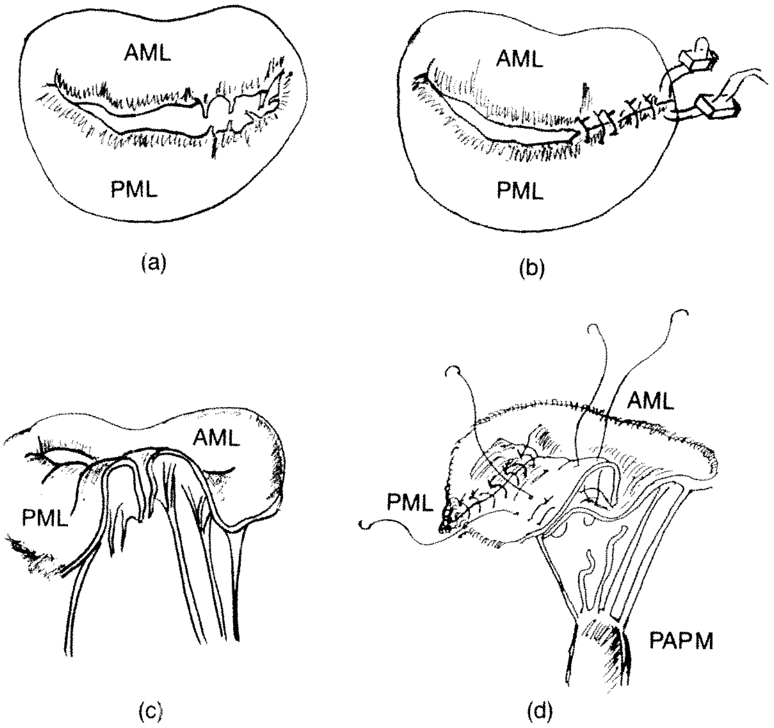
Accepted for publication Aug 25, 1992.

Address reprint requests to Dr Alvarez, Department of Cardiothoracic Surgery, Royal North Shore Hospital, 2065, Sydney, Australia.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Fig 1. Anterior mitral leaflet (AML) *repair techniques: (a) Flail septal component of AML and posterior mitral leaflet* (PML) *with nonredundant leaflet tissue. (b) Septal commissuroplasty: leaflet margins of AML and PML sutured together plus posteromedial annuloplasty. (c) Flail septal components of AML and PML with redundant leaflet tissue. (d) Leaflet repositioning: septal segment of AML sutured beneath septal segment of PML (double-breasting). Quadrangular excision and suture of central segment of PML shown.* (PAPM = *papillary muscle.)*



multifactorial pathology precludes a single procedure to suffice all patients.

With flail septal components involving both leaflets, as an alternative to using Gore-Tex neochordae [3] or secondary chordal translocation [4] we prefer commissuroplasty or double-breasting the leaflets (when the chordae are ruptured). It avoids the difficulty of gauging neochordal length. Concerns about rendering these valves stenotic have not been borne out by our results; admittedly these gradients were calculated at rest, but the postoperative functional class lends support to these valves not being stenotic. The anterolateral segment may be dealt with in this manner.

Table 2. Operative Techniques[a]

Technique	No. of Patients	Percent
Chordal transposition	6	33
Leaflet double-breasting	9	50
Septal commissuroplasty	6	33
AML plication	3	17
Chordal shortening	5	28
Insertion of Duran ring	6	33
PML repair	15	83

[a] All patients had an annuloplasty.

AML = anterior mitral leaflet; PML = posterior mitral leaflet.

Although this a short follow-up we believe this is a technique worth keeping in the armamentarium of the surgeon whose goal is to repair this beautiful structure.

References

1. Brady PW, Deal CW, Angus G. Results of a technique of mitral valve repair. Aust N Z J Med 1987;17:491–4.
2. Duran CG. Repair of anterior mitral leaflet chordal rupture or elongation (the flip over technique). J Cardiac Surg 1986;1:161–6.
3. David TE. Replacement of chordae tendinae with expanded polytetrafluoroethylene sutures. J Cardiac Surg 1989;4:286–90.
4. Deloche A, Jebara VA, Relland JY, et al. Valve repair with Carpentier techniques. The second decade. J Thorac Cardiovasc Surg 1990;99:990–1002.

The Nissen Fundoplication

F. Henry Ellis, Jr, MD, PhD

New England Deaconess Hospital, Harvard Medical School, Boston, Massachusetts

The most commonly employed antireflux operation is the Nissen fundoplication. However, its origin and subsequent modifications are rarely defined. These aspects of the operation are reviewed in this article as are the results currently obtainable with the modern version of the operative procedure.

(Ann Thorac Surg 1992;54:1231–5)

Rudolph Nissen was born in 1896 in Germany, where he underwent his undergraduate medical training (Fig 1). His interest in thoracic surgery was greatly influenced by Professor Sauerbruch, whose assistant he became in 1921 in the surgical department of the University of Munich. He remained there until 1927, when he accompanied Sauerbruch to Berlin, eventually becoming associate professor of surgery at the University of Berlin. In 1933 he was appointed professor and head of the department of surgery at the University of Istanbul in Turkey, but came to the United States during World War II in 1939 where he remained during the war years and their aftermath until 1952. He was first a research fellow in surgery at the Massachusetts General Hospital, but 2 years later became chief of the surgical service at the Jewish Hospital in Brooklyn and subsequently at the Maimondes Hospital in the same city. The culmination of his career was as professor of surgery and head of the department at the University of Basel in Switzerland in 1952, a post that he held until his retirement in 1966. Nissen died on January 22, 1981, at the age of 85 years after a long and productive career, much of it devoted to the field of thoracic surgery, particularly pulmonary surgery.

Although much of Professor Nissen's original pioneering contributions to the field of pulmonary surgery have been forgotten or overlooked, his seminal contribution to the surgical management of selected patients with gastroesophageal reflux disease will long be remembered because his name has become associated with the most widely employed and successful antireflux operation currently in use. The procedure that he first described in 1956 [1] (Fig 2) subsequently underwent modifications by him and his colleagues as well as by others so that the term "Nissen fundoplication" means different things to different people [2]. It is important, therefore, when documenting his position as an innovative antireflux surgeon not only to describe in detail the procedure he originally performed and subsequently modified but also to review the historical setting that led to the introduction of this essentially physiologically based operation.

Historical Setting

Before Nissen's original publication, operations for the repair of diaphragmatic hernia were based on anatomic rather than physiologic principles. It was not then recognized that reflux accounted for the symptoms of a sliding esophageal hiatus hernia, but Nissen [3] ultimately adopted the concepts proposed by Philip Allison in 1951 regarding the nature and relationship of reflux esophagitis to a sliding esophageal hiatus hernia [4]. By the early 1950s he had become dissatisfied with the results of anatomically conceived surgical techniques, including the Harrington and Allison procedures, for a review of his data revealed that 50% of his patients so treated developed either clinical or radiographic failure postoperatively [5]. He therefore sought a more effective procedure, first employing gastropexy in patients with a paraesophageal hiatus hernia in 1946 and later extending its use to elderly poor-risk individuals with a sliding hernia and reflux symptoms [6]. Accentuation of the angle of His by gastropexy was considered by him to explain the symptomatic relief that followed its use in the small number of patients with reflux on whom it was employed. However, he later abandoned the use of gastropexy alone for sliding esophageal hiatus hernia because of a high recurrence rate, 35 of 100 cases [7].

When faced in 1955 with a patient with severe reflux symptoms without a diaphragmatic hernia, Nissen recalled a 28-year-old man with a distal esophageal ulcer penetrating into the pericardium whom he had treated in 1936 by resecting the distal esophagus and proximal stomach. In an effort to protect the anastomotic suture line between esophagus and stomach, he embedded the esophageal stump into the wall of the stomach as in a Witzel gastrostomy [8]. Sixteen years later it was possible to reexamine the patient, and to Nissen's surprise there was no evidence of esophagitis. Thus in December 1955 when confronted with a 49-year-old woman with a 3-year history of reflux esophagitis without a hiatus hernia, he performed a similar type of procedure through a transabdominal approach by mobilizing the distal esophagus and wrapping the distal 6 cm of esophagus with gastric fundus in an effort to correct gastroesophageal reflux. Few details regarding the technique of the operation were provided in his original article [1] (see Fig 2), but subsequent publications in English [9], French [10], and German [11] provided detailed descriptions of the operative procedure (Fig 3).

The phrenoesophageal membrane was divided and the

Address reprint requests to Dr Ellis, Suite 2C, 110 Francis St, Boston, MA 02215.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

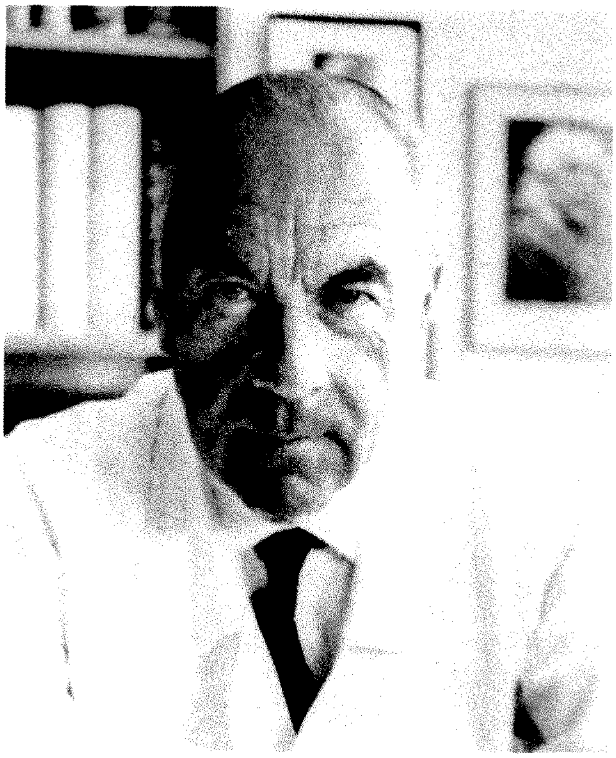


Fig 1. Rudolf Nissen, MD. (Reproduced from Nissen R. Reminiscences—reflux esophagitis and hiatal hernia. Rev Surg 1970;27:307–14, with the permission of the publisher.)

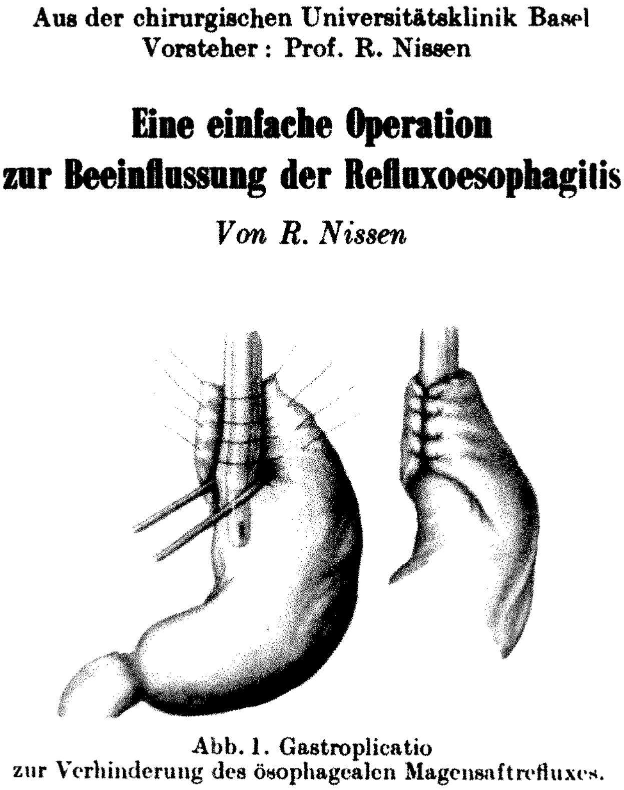
esophagus mobilized to provide a substantial intraabdominal esophageal segment. The gastrohepatic ligament was divided and, if necessary, so was the left gastric artery, but the short gastric vessels were not divided. Then, using the right hand, the gastric fundus was passed behind the stomach and through the opening provided by the divided gastrohepatic ligament to permit encirclement of the distal 6 cm of esophagus. The posterior and anterior walls of the esophagus were then approximated with four or five interrupted sutures, one or more of which also incorporated part of the anterior wall of the esophagus. The wrapping procedure was performed around a large-bore indwelling intraesophageal stent.

Technical Modifications by Nissen and Associates

Although the transabdominal approach was preferred by Nissen, he did not hesitate to use the transthoracic approach under certain circumstances such as a previous failed operation, the presence of a short esophagus, and when other intrathoracic disorders requiring a transthoracic approach were present such as an esophageal ulcer or an epiphrenic diverticulum [12]. Nor did he hesitate to leave the wrap in the chest if it could not be reduced intrabdominally. Although the first operation did not include a gastropexy, the combined operation became the procedure of choice [6] but was gradually abandoned because fundoplication alone proved beneficial. By 1962 gastropexy was no longer combined with fundoplication, being restricted only to patients with a paraesophageal hiatus hernia [9]. Another important modification of the original procedure subsequently became routine practice. In one of the reports by Nissen and Rossetti [7], only the anterior wall of the stomach was used to encircle the distal esophagus in extremely obese patients. This technical modification was described in detail by Rossetti in 1968 [13] and became the procedure of choice in Nissen's clinic. By 1977 Rossetti and Hill [14] were able to report 1,400 cases, many of them operated on using only the anterior wall of the stomach for the wrap. The long-term results in 590 cases were evaluated and symptomatic relief was achieved in 90% of cases. Some time later Rossetti and Hitz [15] further modified the procedure in patients with hyperacidity by performing a vagotomy of the esophagogastric junctional area and bringing the wrap between the vagal trunk and the esophagus.

Other Modifications of the Nissen Fundoplication

There have been many other modifications of the Nissen fundoplication, most of which were designed to avoid some of the complications of the procedure, which include postoperative dysphagia, disruption of the wrap, and the "gas bloat" syndrome, complications related for the most part to the formation of too tight a wrap. Nissen himself originally advocated the use of an indwelling



Aus der chirurgischen Universitätsklinik Basel
Vorsteher: Prof. R. Nissen

Eine einfache Operation
zur Beeinflussung der Refluxoesophagitis

Von R. Nissen

Abb. 1. Gastroplicatio
zur Verhinderung des ösophagealen Magensaftrefluxes.

Fig 2. Title page of Nissen's original article describing his operation and Figure 1 of that article. (Reproduced from Nissen R. Eine einfache Operation zur Beeinflussung der Refluxoesophagitis. Schweiz Med Wochenschr 1956;86:590–2, by permission.)

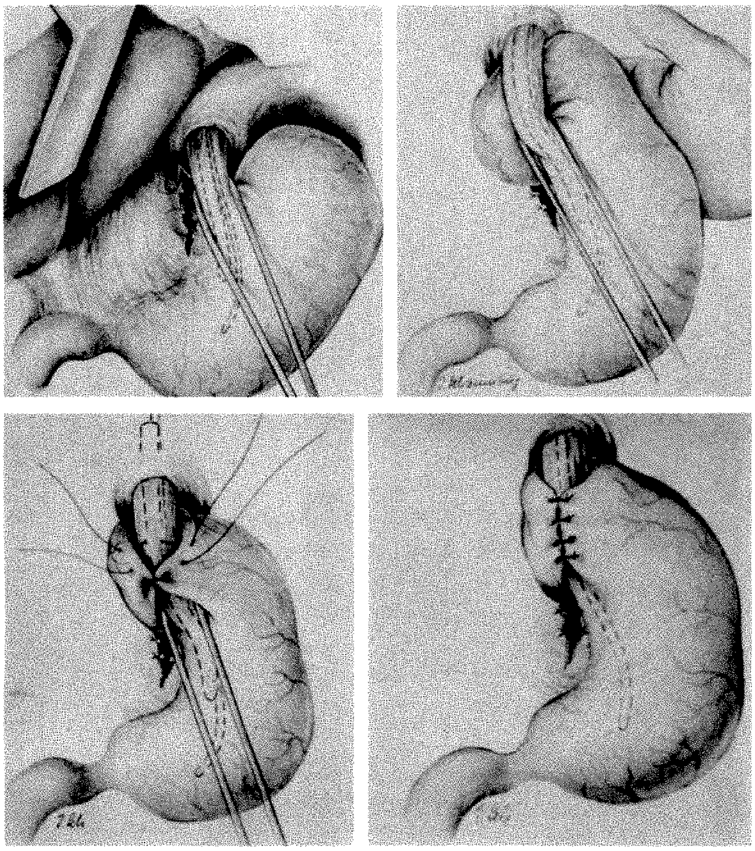


Fig 3. Detailed illustrations of the Nissen fundoplication. (Reproduced from Nissen R. The treatment of hiatal hernia and esophageal reflux by fundoplication. In Nyhus LM, Harkins HH, eds. Hernia. Philadelphia: J.B. Lippincott, 1964:488–96, by permission.)

stent during the performance of the wrap, and this maneuver is currently employed by most surgeons performing the operation, although the size of the stent varies with the operator. I employ a 46F to 50F Maloney dilator depending on the size of the patient, but some advocate using a larger stunt, up to 60F [16]. Although the original Nissen procedure did not involve division of the short gastric and posterior gastric vessels, complete mobilization of the fundus by division of these vessels is now preferred by most surgeons to provide as loose a wrap as possible in an effort to avoid the complications just mentioned. The advantages of a loose, "floppy" wrap in avoiding the gas bloat syndrome have been well documented [17]. Division of the gastrohepatic ligament, advocated by Nissen, is now rarely performed not only to preserve the hepatic branch of the vagus nerve but to prevent caudal migration of the wrap. Some prefer to exclude one or both vagus nerves from the wrap [15, 18, 19]. Whereas Nissen's original wrap extended over 6 cm of the distal esophagus, most surgeons now prefer a shorter wrap as recommended by DeMeester and associates [20], the wrap enveloping only 1 to 2 cm of the distal esophagus. Other modifications include narrowing of the esophageal hiatus [21], anchoring of the plication sutures to the preaortic fascia [22] to prevent mediastinal migration of the wrap, concomitant performance of parietal cell vagotomy (not only to reduce gastric acidity, but also to simplify performance of the fundoplication) [23], and decreasing the degree of the fundal wrap to encircle less than 360 degrees of the esophageal tube. The partial wrap was proposed in an effort to minimize the risk of postoperative gas bloat syndrome. The names of Guarner [24], Dor [25], and Toupet [26] have become associated with such procedures depending on whether the partial wrap is applied anterior to the esophagus or posterior to it. Other modifications include the cut or uncut Collis-Nissen procedures for reflux associated with a shortened esophagus and the Thal-Nissen for relief of obstruction and reflux in the presence of a peptic esophageal stricture.

Mechanism of Action of Fundoplication

It is not clear from Nissen's articles how he believed his fundoplication prevented reflux. Esophageal manometry was not part of his preoperative or postoperative workup and apparently never became so. Certainly restoration of normal anatomy was not his goal, as it was for Belsey and Hill with their procedures, although both accomplish a modified wrap. Perhaps he thought he was fashioning a "flutter valve," a mechanism suggested by others [27]. However, regardless of which modification of the Nissen fundoplication is employed, the mechanism by which the wrap accomplishes its antireflux function is probably the same. A variety of explanations for its mode of action have been suggested. Most postoperative manometric studies identify an increase in amplitude and length of the high-pressure zone after the performance of fundoplication [28–30]. This has been explained on the basis of purely mechanical factors by the experimental studies of Condon and associates [31]. In addition to the mechanical effect of fundoplication there is a return to normal of the adaptive response of the response of the lower esophageal sphincter (LES) to graded increases in intragastric pressure suggesting a return of the normal physiology of the sphincter mechanism [32]. Furthermore, the subnormal response of the hypotensive LES to gastrin administered parenterally is restored to normal after clinical fundoplication and experimental fundoplication [33], suggesting that the smooth muscle of the gastric fundus behaves in a manner similar to the smooth muscle of the LES, a concept supported by the anatomic studies of Liebermann-Meffert [34]. Lipschutz and associates [35] have suggested that alteration in the length tension characteristics of the LES produced by the surgical repair is an important factor in preventing reflux. It has also been suggested that antireflux operations may interrupt distracting forces on the LES by limiting tension at the gastroesophageal junction [36]. Thus there are a multiplicity of explanations for the successful antireflux function of fundoplication procedures, none of which have been convincingly proved to be the true mechanism. In all likelihood, a variety of factors are involved in the success of fundoplication procedures in preventing reflux. Suffice it to say, Nissen was the first of the antireflux surgeons to attempt to restore normal physiology, not normal anatomy.

Current Results of the Modified Nissen Fundoplication

It is difficult to evaluate the reported results of the modified Nissen fundoplication because of differences in methods of reporting, varying patient populations, and the subtle variations in the surgical techniques employed. In general, however, successful alleviation of reflux symptoms has been achieved in from 85% to 90% of patients [20, 32]. Negre [37], however, has drawn attention to the high frequency of complications following this operation. Of 226 patients followed up, 19% had persistent or recurrent reflux and only 24% were totally without symptoms. Such findings have not been the universal experience, however, as suggested by another recent study which followed up 350 patients up to 20 years after the Nissen fundoplication and found a low incidence of complications, only 5.7% of patients exhibiting the gas bloat syndrome, 2.9% complaining of dysphagia, and only 4.8% having recurrent reflux [38].

A number of studies, some of which were prospective and randomized, have compared the results of the Nissen procedure with those of other antireflux operations such as the Belsey, Hill, and Toupet procedures. With few exceptions [39–41], these studies have found Nissen fundoplication to be superior to the other operations in restoring LES function and preventing reflux [29, 42–44]. Even more important is a recent study involving a long-term randomized comparison of the results of medical therapy with the Nissen fundoplication for patients with complicated gastroesophageal reflux disease. The conclusion from this study was that operation was significantly more effective than medical therapy in improving the symptoms and endoscopic signs of esophagitis [45].

In summarizing the pertinent recent literature on the results of the modified Nissen fundoplication, one is drawn to the conclusion that with proper patient selection and the use of meticulous surgical technique emphasizing a short loose total wrap, the Nissen fundoplication will provide relief of symptoms in approximately 90% of patients with a low incidence of serious side effects. Whether the indications for surgical therapy will persist at the present level now that H_2 receptor antagonists and omeprazole (Prilosec), an effective proton pump inhibitor, are available remains to be seen. A recent report from a major surgical referral center in Great Britain describes an 87.5% reduction in the numbers of patients being referred for antireflux operation since the introduction of H_2 receptor antagonists [46]. All the same, as long as there are medical failures and uncertainties regarding potential adverse effects of long-term administration of the new antisecretory drugs, modifications of Nissen's originally proposed operation will be the procedure of choice to provide reflux control in appropriately selected patients with the complications of gastroesophageal reflux disease.

The assistance of Professor Andre P. Naef and Paul A. Kirschner in the preparation of the historical aspects of this review is gratefully acknowledged.

References

1. Nissen R. Eine einfache Operation zur Beeinflussung der Refluxoesophagitis. Schweiz Med Wochenschr 1956;86:590–2.
2. Jamieson GG, Duranceau A. What is a Nissen fundoplication? Surg Gynecol Obstet 1984;159:591–3.
3. Nissen R. Beiziehungen zwischen Hiatushernie und Refluxoesophagitis. Munchen Med Wochenschr 1960;102:1472–4.
4. Allison R. Reflux esophagitis, sliding hiatal hernia and anatomy of repair. Surg Gynecol Obstet 1951;92:419–31.
5. Nissen R. Gastropexy as lone procedure in surgical repair of hiatus hernia. Am J Surg 1956;92:389–92.
6. Nissen R. Gastropexy and "fundoplication" in surgical treatment of hiatal hernia. Am J Dig Dis 1961;6:954–61.
7. Nissen R, Rossetti M. Surgery of hiatal and other diaphragmatic hernias. J Int Coll Surg 1965;43:663–74.
8. Nissen R. Die transpleurael Resektion der Kardia. Deutsche Z Chir 1937;249:311–6.
9. Nissen R. The treatment of hiatal hernia and esophageal reflux by fundoplication. In: Nyhus LM, Harkins HH, eds. Hernia. Philadelphia: J.B. Lippincott, 1964:488–96.
10. Nissen R, Rossetti M. La fundoplicatio et la gastropexie dans le traitement chirurgical de l'insuffisance du cardia et de la hernie hiatal. Ann Chir 1962;16:825–36.
11. Nissen R, Rossetti M. Die Behandlung von Hiatushernien und Refluxoesophagitis mit Gastropexie und Fundoplication. Stuttgart: Thieme, 1959.
12. Nissen R. Transthorakale Fundusrafflung zur Beeinflussung besonderer Formen von Refluxoesophagitis. Langenbechs Arch Klin Chir 1960;293:365–72.
13. Rossetti M. Zur Technic der Fundoplicatio. Actuelle Chir 1968;3:29.
14. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. World J Surg 1977;1:439.

15. Rossetti M, Hitz P. Intravagale Fundoplicatio und kardiofundale Vagotomie: eine Technisch-physiologische Variante in der Refluxchirurgie. Helv Chir Acta 1989;55:559–64.
16. DeMeester TR, Stein HJ. Minimizing the side effects of antireflux surgery. World J Surg 1992;16:335–6.
17. Donahue PE, Samelson S, Nyhus LM, Bombeck CT. The floppy Nissen fundoplication: effective long term control of pathologic reflux. Arch Surg 1985;120:663–7.
18. Herrington JL Jr, Meacham PW, Hunter RM. Gastric ulceration after fundic wrapping. Vagal nerve entrapment, a progressive causative factor. Ann Surg 1982;195:574–81.
19. Siewert JR, Feussner H, Walker SJ. Fundoplication: how to do it? Peri-esophageal wrapping as a therapeutic principle in gastro-esophageal reflux prevention. World J Surg 1992;16:326–34.
20. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. Ann Surg 1986;204:9–20.
21. Ellis FH Jr. Nissen fundoplication. In: Braasch JW, et al eds. Atlas of abdominal surgery. Philadelphia: Saunders, 1990:10–6.
22. Codiano C, Revere GQ, Agugiaro S, et al. Technical modification of the Nissen fundoplication procedure. Surg Gynecol Obstet 1976;143:977–8.
23. Jordan PH Jr. Parietal cell vagotomy facilitates fundoplication in the treatment of reflux esophagitis. Surg Gynecol Obstet 1978;147:593–5.
24. Guarner V, Martinez N, Gavino JF. Ten year evaluation of posterior fundoplasty in the treatment of gastroesophageal reflux: long term and comparative study of 135 patients. Am J Surg 1980;139:200–3.
25. Dor J, Humbert P, Dor V, Figarella J. L'intérét de la technique de Nissen modifiée la prevention du reflux après cardiomyotomie extra muqueuse de Heller. Mem Acad Chir 1962;88:877–83.
26. Toupet A. Technique d'oesophagogastroplastie avec phrenogastropexie appliquée dans la cure radicale des hernia hiatales et comme complement de l'operation de Heller dans les cardiospasmus. Mem Acad Chir 1963;89:374–9.
27. Matikainen M, Kaukinen L. The mechanism of Nissen fundoplication. Acta Chir Scand 1984;150:653–5.
28. Ellis FH Jr, El-Kurd MF, Gibb SP. The effect of fundoplication on the lower esophageal sphincter. Surg Gynecol Obstet 1976;143:1–5.
29. DeMeester TR, Johnson FF, Kent AH. Evaluation of current operations for the prevention of gastroesophageal reflux. Ann Surg 1974;180:511–23.
30. Csendes A, Braghetto J, Korn O, Cortes C. Late subjective and objective evaluations of antireflux surgery in patients with reflux esophagitis. Analysis of 215 patients. Surgery 1989;105:374–82.
31. Condon RE, Kraus MA, Wolheim D. Cause of increase in "lower esophageal sphincter" pressure after fundoplication. J Surg Res 1976;20:445–50.
32. Ellis FH Jr, Crozier RE. Reflux control by fundoplication: a clinical and manometric assessment of the Nissen operation. Ann Thorac Surg 1984;38:387–92.
33. Siewert R, Jennewein HM, Waldeck F, et al. Experiementelle und klinische Untersuchungen zum Wirkungsmechanismus der Fundoplicatio. Langenbecks Arch Chir 1973;333:519–22.
34. Liebermann-Meffert D. Architecture of the musculature of the gastroesophageal junction and in the fundus. Chir Gastroenterol 1975;9:425–9.
35. Lipshutz WH, Eckert RJ, Gaskins RD, et al. Normal lower esophageal sphincter function after surgical treatment of gastroesophageal reflux. N Engl J Med 1974;291:1107–10.
36. Anderson KW, Bombeck CT. Why anti-reflux surgery works. Surg Rounds 1987;11:49.
37. Negre JB. Post-fundoplication symptoms: do they restrict the success of Nissen fundoplication? Ann Surg 1983;198:698–700.
38. Shiraz SS, Schulze K, Soper RT. Long term follow-up for treatment of complications of reflux oesophagitis. Arch Surg 1987;122:548–52.
39. Fenaris VA, Sube J. Retrospective study of the surgical management of reflux esophagitis. Surg Gynecol Obstet 1981;152:17–21.
40. Thor KBA, Selander T. A long term randomized prospective trial of the Nissen procedure versus a modified Toupet technique. Ann Surg 1989;210:719–24.
41. Stipa S, Fegiz G, Iascone C, et al. Belsey and Nissen operations for gastroesophageal reflux. Ann Surg 1989;210:583–9.
42. Nicholson DA, Nohl-Oser HC. Hiatus hernia: a comparison between two methods of fundoplication by evaluation of the long term results. J Thorac Cardiovasc Surg 1976;72:938–43.
43. Dilling EW, Peyton MD, Cannon SP, et al. Comparison of Nissen fundoplication and Belsey Mark IV in the management of gastroesophageal reflux. Am J Surg 1973;134:730–3.
44. Sillin LF, Condon RE, Wilson SD, Worman LW. Effective surgical therapy of esophagitis: experience with Belsey, Hill and Nissen operations. Arch Surg 1979;114:536–40.
45. Spechler SJ. Comparison of medical and surgical therapy for complicated gastroesophageal reflux disease in veterans. N Engl J Med 1992;326:786–92.
46. Macintyre IMC, Goulbourne IA. Long term results after Nissen fundoplication: a 5–15 year review. J R Coll Surg Edinb 1990;35:159–62.

Release of Vasoactive Substances During Cardiopulmonary Bypass

Stephen W. Downing, MD, and L. Henry Edmunds, Jr, MD

Division of Cardiothoracic Surgery, Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Cardiopulmonary bypass is associated with bleeding and thrombotic complications, massive fluid shifts, and cellular and hormonal defense reactions that are collectively termed "the whole body inflammatory response." A host of vasoactive substances are produced, released or altered during cardiopulmonary bypass. These hormones, autacoids, and cytokines react with specific receptor proteins distributed throughout the body, and mediate the vascular smooth muscle and endothelial cell contractions that are responsible for much of the morbidity associated with open heart operations. This essay briefly reviews the actions, sources, and perturbations of the approximately 25 vasoactive substances known or believed to be altered by cardiopulmonary bypass, and provides an introductory reference list.

(Ann Thorac Surg 1992;54:1236–43)

Cardiopulmonary bypass (CPB) exposes blood to large areas of synthetic materials and triggers the production and release of numerous vasoactive substances from cellular deposits and whole organs. These vasoactive substances affect local and systemic vascular resistance, vascular permeability, fluid balance, and myocardial contractile force and contribute to the "whole body inflammatory response" associated with CPB [1]. Rapid development of new immunochemical assays and heightened interest in the pathophysiology of CPB have accelerated discoveries of vasoactive compounds altered by CPB. Many of these changes are well documented; others await documentation but are likely based on circumstantial evidence. This essay offers a brief but necessarily temporal review of this rapidly unfolding subject.

Hormones, autacoids, and cytokines are the mediators of endothelial cell and vascular smooth muscle contraction [2]. As far as we know, CPB does not activate lymphocytes or production of immunoglobulins [3]. Hormones, produced by specialized organs and cells, and plasma autacoids circulate; other autacoids and cytokines normally are local mediators of inflammation. Cytokines, platelet activating factor, and the eicosanoids are nonantibody peptides or phospholipids that are produced in response to specific agonists by cells that circulate (eg, white blood cells) or that are nearly ubiquitous (eg, endothelial cells). Hormones, autacoids, and cytokines all act on specific receptor proteins distributed on different cells throughout the body. Thus when CPB simultaneously and vigorously stimulates the production and release of a host of vasoactive substances, a massive whole body inflammatory response is initiated (Table 1).

Sympathetic Amines

Epinephrine, norepinephrine, and dopamine are endogenous catecholamines with powerful vasoactive properties [2]. Epinephrine, produced in the adrenal medulla, is primarily a β-agonist and increases heart rate, contractile force, and cardiac output. Epinephrine also increases blood pressure and skeletal muscle blood flow but decreases renal and skin flow. Norepinephrine is primarily an α-agonist and is produced and released from sympathetic nerve terminals. Norepinephrine can increase stroke volume but also increases peripheral vascular resistance and blood pressure so that cardiac output is usually not increased. Dopamine is also produced in the adrenal medulla, and has primarily β-adrenergic effects at low concentrations and α-adrenergic effects at high concentrations. Dopamine also stimulates D1 receptors to increase renal and mesenteric blood flow.

Cardiopulmonary bypass does not alter plasma concentrations of dopamine [4]. Anesthesia and operation raise epinephrine and norepinephrine concentrations. With CPB, the plasma epinephrine level progressively increases from 150 to 600 pg/mL [3, 4]. The norepinephrine level increases from 200 to 700 pg/mL [4–6]. With reperfusion of the lungs, epinephrine and norepinephrine concentrations decrease [6] but do not return to normal concentrations for 24 hours. Deep hypothermia with circulatory arrest produces even greater concentrations of sympathetic amines, with the highest levels reached during rewarming (mean epinephrine level, 3,724 pg/mL; norepinephrine, 4,543 pg/mL) [7].

Renin, Angiotensin, and Aldosterone

Renin is released from the juxtaglomerular cells in the renal cortex in response to changes in renal perfusion pressure, β-receptor stimulation, and tubular sodium content. Renin converts angiotensinogen into angiotensin I, which is converted in the lungs to vasoactive angioten-

---

Address reprint requests to Dr Edmunds, Department of Surgery, Hospital of the University of Pennsylvania, 3400 Spruce St, Philadelphia, PA 19104.

© 1992 by The Society of Thoracic Surgeons

0003-4975/92/$5.00

Table 1. Vasoactive Substances Released During Cardiopulmonary Bypass

Substance	Primary Source	Vasoactive Effects	Early[a]	Late[b]	References	Comments
Epinephrine	Adrenal medulla	↑ HR, inotrope, ↑ muscle blood flow, ↓ renal and skin blood flow	↑ ↑	↑	4–7	Drops with lung reperfusion, highest levels seen with deep hypothermia
Norepinephrine	Sympathetic nerves	↑ SV, SVR, BP	↑ ↑	↑	4–7	
Dopamine	Adrenal medulla	Dose-dependent α and β effects, ↑ renal and mesenteric blood flow	↔	↔	4	
Renin	Juxtaglomerular cells in renal cortex	Converts angiotensinogen to angiotensin I	↔ or ↑	↔ or ↑	4, 8–10	Release decreased by β-blockers and hypothermia
Angiotensin II	Lungs (via converting angiotensin I)	Potent vasoconstrictor, aldosterone release	↔ or ↑	↔ or ↑	11–13	See text
Aldosterone	Adrenal cortex	↑ sodium and fluid retention	↑ ↑	↔	14, 15	Affected by potassium levels
Vasopressin	Posterior pituitary	↑ water and sodium resorption	↑ ↑	↔ or ↑	13, 15–18	Vasoconstriction and paradoxical diuresis seen at higher levels
Atrial natriuretic factor	Atria	↑ sodium excretion, ↓ aldosterone, vasodilator	↔ or ↑	↑ ↑	15, 19, 20	Correlation with atrial pressure lost for 24 hours
Bradykinin	Blood; high-molecular-weight kininogen	Vasodilator, ↑ capillary permeability	↑ ↑	↑	20–23	Cleared by pulmonary converting enzymes
Thyroxine	Thyroid	Converted to triiodothyronine	↔ or ↑	↔ or ↑	24–27	Refers to free fraction only
Triiodothyronine	Thyroid	↓ SVR, ↑ HR and CO	↓	↓	24–27	Refers to free fraction only
Glucagon	Pancreas	Inotrope	↑ ↑	↑ or ↑ ↑	28	
Calcium		Inotrope	↔ or ↑, ↓	↔	29, 30	Plasma concentration varies during CPB
Potassium		↓ contractility, arrhythmias	↔ or ↑, ↓	↔	29, 30	As above
Magnesium		Arrythmias	↔ or ↑, ↓	↔	29, 30	As above
C3a	Blood; complement	↑ vascular permeability, hypotension, ↑ HR, coronary vasoconstriction, ↓ contractility	↑ ↑	↑ ↑	31–36	Effects mediated by activation of leukocytes
C4a, C5a	Blood; complement, leukocytes	↑ vascular permeability, hypotension	↔ or ↑	↑	31–36	As above
Platelet activating factor	Leukocytes, mesangial cells, endothelium	Platelet and leukocyte aggregation, vasodilation, ↑ vascular permeability	↑ ↑		37, 38	Also stimulates thromboxane, leukotrienes, platelet factor 4, IL-1, proteases, and superoxide radicals
Prostaglandin E_2	Lung	Vasodilation	↑ ↑	↔	2, 38	Also metabolized in lung
Prostaglandin I_2 (prostacyclin)	Endothelium	Vasodilation and platelet inhibition	↑ ↑	↑	2, 38, 39	Short half-life in plasma
Thromboxane A_2	Platelets	Vasoconstriction	↑ ↑	↔	37–40	Short half-life in plasma
Leukotrienes LTB4, LTC4, LTD4	WBCs	Vasocontriction, ↑ capillary permeability, coronary vasoconstriction, ↓ GFR			2, 39–44	Change during CPB not documented
Endothelin-1	Endothelium	Vasoconstriction	↑ ↑	↑ or ↔	45–47	10-fold more potent than angiotensin II
Nitric oxide	Endothelium, leukocytes	Vasodilation			45, 48, 49	Change during CPB not documented
Serotonin	Platelets	Vasoconstriction, ↑ BP, HR, contractility	↔ or ↑	↔ or ↑	2, 45, 50–53	Serotonin formed in gut and carried by platelets
Free O_2 radicals, lysosomal enzymes, proteases	Leukocytes	↑ vascular permeability endothelial damage	↑ ↑		2, 5, 34, 35, 54–61	Significant accumulation in and damage to lungs
Interleukin-1	Monocytes	Inflammatory mediator, ↓ SVR, ↑ permeability	↔	↑ ↑	48	
Histamine	Mast cells, basophils	↑ capillary permeability, small vessel dilation	↑		62, 63	

[a] During CPB. [b] For up to 24 hours after CPB.

BP = blood pressure; CO = cardiac output; CPB = cardiopulmonary bypass; GFR = glomerular filtration rate; HR = heart rate; IL-1 = interleukin-1; SV = stroke volume; SVR = systemic vascular resistance; WBCs = white blood cells; ↑ ↑ = increased; ↑ = slightly increased; ↔ = no change; ↓ = decreased.

sin II by angiotensin converting enzyme [2]. Angiotensin II is a potent vasoconstrictor, stimulates aldosterone secretion, and increases sympathetic activity. The renin level remains unchanged [4, 8–10] or increases only slightly during and after CPB [11, 14, 64]. Both β-blockers and hypothermia decrease renin release [11, 65]. Although Taylor and associates [12, 66, 67] have shown an increase in angiotensin II from 50 to around 250 pg/mL during CPB, others have shown no increase or a net decrease [11, 14] unless significant hypotension is artificially induced [13]. These discrepant observations are probably due to variable renin release, pulmonary blood flow, and angiotensin converting enzyme activity during CPB. Systemic concentrations of angiotensin converting enzyme decrease by one-third during CPB [68]. The level of aldosterone, which technically is not vasoactive, increases from approximately 5 to 18 ng/dL during CPB and returns to normal by 3 hours postoperatively [14, 15]. The aldosterone level is also influenced by potassium levels.

Vasopressin

Vasopressin (antidiuretic hormone) is released from the posterior pituitary primarily in response to changes in serum osmolality [2]. Release is also affected by changes in blood volume, blood pressure, pain, and visceral stimulation. Vasopressin increases water absorption in distal renal collecting tubules, and to a lesser extent alters sodium resorption. Cardiopulmonary bypass increases the concentration of vasopressin from approximately 2 pg/mL to a range of 16 to 80 pg/mL within the first 10 to 30 minutes [13, 15–18]. These concentrations diminish slightly over time, then drop more sharply with cessation of CPB [13, 17]. Postoperative measurements conflict; some show a return to baseline vasopressin levels [15], and others show a second substantial increase in the first few hours [13, 17]. At the supraphysiologic concentrations (>15 pg/mL) reached during CPB, vasopressin has a paradoxical diuretic effect [65] and also becomes a potent systemic and coronary vasoconstrictor [16]. Elevations in vasopressin levels correlate with decreases in blood pressure during CPB [18].

Atrial Natriuretic Factor

This small peptide is released from the atrium in response to distention and stimulates renal excretion of sodium, inhibits aldosterone release, and dilates vascular smooth muscle [2]. Despite atrial manipulations, the level of plasma atrial natriuretic factor decreases with CPB [19] or increases slightly after correction for dilution [15, 20]. Secretion of atrial natriuretic factor decreases with hypothermia and increases with rewarming [19]. Postoperatively, atrial natriuretic factor levels increase from a range of 40 to 150 pg/mL to a range of 78 to 350 pg/mL but correlate poorly with atrial pressure for at least 24 hours [15, 19, 20].

Bradykinin

This small vasoactive peptide is produced by cleavage of high-molecular-weight kininogen by kallikrein during activation of the contact system. In vitro the contact system is also activated by cold [21]. Bradykinin is a classic inflammatory mediator; it is a powerful vasodilator, increases capillary permability, and participates in local hyperemia. It has a half-life of 18 to 24 seconds [22] and is degraded by pulmonary converting enzymes [21–23]. Angiotensin converting enzyme, which is located on the outer surface of endothelial cells, inactivates bradykinin in peripheral tissues. The bradykinin level is elevated by simple surface cooling of infants from 1.1 to 2.1 ng/mL [21]. During CPB, which activates the contact system and excludes the lungs, the bradykinin level progressively increases to between 5 and 10 ng/mL [20–22], and the kininogen level drops reciprocally from 7 to 3 μg/mL [23]. Bradykinin levels return to near normal shortly after bypass stops.

Thyroid Hormones

The thyroid gland secretes both thyroxine and triiodothyronine (T_3). Both hormones are active, but most plasma thyroxine is converted to T_3 in peripheral tissues [2]. Triiodothyronine binds to the cell nucleus, mitochondria, certain cytosolic proteins, and probably also cell membrane [24]. The complex reactions of this hormone are not completely understood. Triiodothyronine increases adenosine triphosphate production by mitochondria and increases metabolic rate and heat production. Triiodothyronine reduces systemic vascular resistance and increases heart rate. Cardiac output increases, but it is not clear that T_3 has a direct inotropic effect on the heart or whether it works indirectly by reducing afterload. There is evidence that T_3 affects calcium flux at the myocyte cell membrane. The late effects of T_3 are primarily due to alterations in DNA transcription and increased synthesis of protein and cytosolic messenger RNA.

During and after CPB, the total thyroxine level decreases slightly but remains within the normal range [25–27]. The free thyroxine level does not change [26] or increases slightly [25]. The total T_3 level decreases significantly soon after CPB starts [25–27] and falls near [25, 27] or below [26] normal limits. The free T_3 level decreases at the beginning of bypass [25, 26], and after bypass ends it falls below normal values for at least 24 hours [26]. The level of plasma thyroid stimulating hormone changes during and after bypass, but the changes vary between studies [25–27] and all remain within the normal range.

Glucagon

Glucagon, in addition to its role in glucose metabolism, is a stress hormone and cardiac inotrope [69]. The hormone can increase intracellular cyclic 3′,5′ adenosine monophosphate levels, even in the presence of β-blockade. During CPB, the glucagon level increases from approximately 100 to 200 pg/mL, and it remains elevated for more than 48 hours after operation [28].

Electrolytes

Bypass also alters plasma electrolytes, and potassium, calcium, and magnesium have cardiovascular effects. Potassium is a negative inotrope and has an indirect effect on intracellular calcium [2]. Calcium is a positive inotrope and a weak vasoconstrictor. Magnesium antagonizes some actions of calcium [29]. Many variables alter plasma electrolyte levels during CPB. Levels of potassium and to a lesser extent calcium are monitored carefully during and after CPB and both are maintained within the normal range. Hyperkalemia is aggressively treated by diuretics, bicarbonate, insulin, and glucose and occasionally dialysis during CPB. Magnesium is sometimes added to cardioplegic solutions to minimize deleterious effects of intracellular calcium. The plasma magnesium level generally decreases during and after bypass [30], and deficiency may contribute to difficult ventricular arrhythmias.

Complement

The interaction of blood and the synthetic surfaces of the perfusion circuit activates factor XII (Hageman factor) and the contact activation system. This system contains four primary proteins: factor XII, factor XI, prekallikrein, and high-molecular-weight kininogen. Activation of factor XI initiates the coagulation cascade; cleavage of high-molecular-weight kininogen by kallikrein produces bradykinin. Cleavage of plasminogen by kallikrein (weakly) and tissue plasminogen activator, which is produced by endothelial cells, produces the fibrinolytic enzyme plasmin.

Activation of the contact system also activates the first component of complement, C1, by formation of activated factor XII fragments, XIIa and XIIf. Activation of the complement cascade via either the classic or alternative pathways (there is evidence that both pathways are activated during cardiopulmonary bypass) leads to formation of C3a, C4a, and C5a. These complement fragments are anaphylatoxins that increase vascular permeability, release histamine from mast cells, and cause hypotension and contraction of airway smooth muscle [31, 32]. C3a also causes cardiac dysfunction manifested by tachycardia, coronary vasoconstriction, and reduced contractility [33]. These actions occur at physiologic concentrations of C3a and are probably mediated by release of leukotrienes, histamine, and platelet activating factor [33]. C5a rapidly binds to white blood cells [34], and measurements vary during cardiopulmonary bypass [34–36]. Plasma C3a concentrations increase progressively during bypass [34] and remain elevated more than 3 hours after bypass before decreasing to normal levels within 10 to 12 hours [36]. Plasma C4a concentrations do not increase during CPB but increase significantly immediately afterward [35].

Platelet Activating Factor

Platelet activating factor is a phospholipid autacoid produced by neutrophils, monocytes, eosinophils, mast cells, glomerular mesangial cells, and endothelial cells [2, 70] but not platelets in response to various stimuli including thrombin, complement, vasopressin, angiotensin II, bradykinin, leukotrienes, adenosine triphosphate, and cardiopulmonary bypass [36, 70]. The primary action of platelet activating factor appears to be amplification of platelet and leukocyte responses during thrombosis, shock, anaphylaxis, and local inflammation. Platelet activating factor stimulates platelet and leukocyte aggregation and release, is a potent vasodilator, and increases vascular permeability [2, 70]. Platelet activating factor stimulates thromboxane, leukotriene and interleukin-1 production and release of platelet factor 4, superoxide radicals, and various proteases and cytokines [70]. Platelet activating factor binds to specific cellular receptors and is metabolized by cellular membrane and cytosolic enzymes more slowly than most other autacoids [70]. In 7 patients, CPB increased platelet activating factor threefold to fourfold 24 hours after operation [37].

Eicosanoids

The eicosanoids are autacoids that can be produced by nearly every mammalian cell in response to stimulation but are not stored [2]. Normally, these compounds do not circulate, but act locally at or near their sites of production. This family of vasoactive phospholipids is derived from arachidonic acid, which is metabolized by either cyclooxygenase, which produces the prostanoids and is irreversibly inhibited by aspirin, or lipooxygenase, which produces the leukotrienes (LTs) [2]. The most important prostanoids are prostaglandin E_2 (PGE_2), PGI_2 (prostacyclin), and thromboxane A_2. The most important leukotrienes are LTB_4, LTC_4, and LTD_4.

Prostaglandin E_2 is primarily produced and metabolized in the lung [2] and is a powerful vasodilator that acts on arterioles and precapillary and postcapillary sphincters. The level of prostaglandin E_2 increases abruptly when CPB starts and decreases quickly when bypass ends [38].

Prostacyclin is primarily produced by endothelial cells and is not normally produced by platelets [2]. Prostacyclin is also a vasodilator and is approximately 5 times more potent than PGE_2. Prostacyclin is also a potent inhibitor of platelet aggregation. This autacoid has a short half-life in plasma (<3 minutes) and is excreted in urine principally as 6-keto-$PGF_{1\alpha}$ [2]. Cardiopulmonary bypass causes a sharp increase in the PGI_2 level during cannulation and the start of bypass; thereafter, prostacyclin concentrations decrease progressively during and after CPB [38, 39].

Thromboxane A_2 is a powerful vasoconstrictor and is primarily produced by platelets. Thromboxane A_2 also is a strong agonist for platelet aggregation and release, and may be the principal physiologic agonist [2]. The compound has a short half-life in plasma (<3 minutes) and is rapidly metabolized to thromboxane B_2, which is stable. Cardiopulmonary bypass activates platelets as soon as blood contacts synthetic surfaces, and thromboxane B_2 appears within the perfusate in 1 to 2 minutes [37]. During clinical CPB, thromboxane B_2 concentrations more than double, but they fall rapidly after bypass ends [38, 39, 40, 71]. Studies differ as to when peak concentrations occur [38, 39, 40, 71].

The leukotrienes are primarily produced in varying concentrations by neutrophils, eosinophils, monocytes, and macrophages, and by mast cells via the lipoxygenase pathway [41, 42]. Neutrophils produce LTA_4, which is converted within the cell to LTB_4, a chemotactic protein that activates endothelial cell adhesive receptors [2, 41]. Monocytes also produce LTB_4, but eosinophils and mast cells do not [41, 42]. Leukotriene C_4, LTD_4, and the less potent LTE_4 are formed from LTA_4 by LTC_4 synthase, which neutrophils lack [2, 41] but monocytes, eosinophils, mast cells, and endothelial cells have. Endothelial cells cannot make LTA_4 but use LTA_4 made by neutrophils to produce with eosinophils, monocytes, and macrophages and mast cells the potent vasoactive leukotrienes LTC_4 and LTD_4 [41, 42]. These phospholipids cause bronchoconstriction and arterial and arteriolar vasoconstriction, and increase vascular permeability by contracting endothelial cells [2, 41, 42]. Coronary arterial vasoconstriction produced by the leukotrienes reduces myocardial contractility [39, 71], and renal vascular constriction reduces glomerular filtration.

An increase in leukotrienes has not been documented during CPB, although there is ample evidence of neutrophil, monocyte, and endothelial cell activation by release of elastase, lactoferrin, and myeloperoxidase (neutrophils) [43, 72], interleukin-1 (monocytes) [48], and tissue plasminogen activator (endothelial cells) [49]. Thus it is likely that CPB stimulates leukotriene production.

Endothelial Cells

The mechanism by which endothelial cells are activated by CPB is not known. However, endothelial cells are activated by both mechanical and diverse chemical stimuli such as thrombin, bradykinin, and epinephrine [45, 49]. Endothelial cells produce at least four vasoactive substances: platelet activating factor, PGI_2, nitric oxide, and endothelin-1. Platelet activating factor and PGI are discussed above; the others are considered here.

Nitric oxide, formerly known as endothelial derived relaxing factor, is formed from L-arginine by endothelial cells, macrophages, neutrophils, certain neurons, and a few other cells [45, 49]. Nitric oxide relaxes vascular smooth muscle by causing production of intracellular cyclic guanosine monophosphate [49]. Nitric oxide acts only locally, is inactivated by hemoglobin, and disappears within seconds [45]. However, its continual synthesis and release by endothelial cells dilates the entire vascular system; inhibition of nitric oxide formation increases blood pressure [49]. Nitric oxide works synergistically with PGI_2 to control platelet activation.

Nitric oxide is also cytotoxic and is produced for that purpose by neutrophils, macrophages, and other killer cells [45]. Production of nitric oxide increases dramatically with infection.

There is no direct evidence that CPB changes nitric oxide production. However, high shear stress in arteries stimulates endothelial cell synthesis of nitric oxide [48]. Furthermore, neutrophils and monocytes activated by CPB likely produce and release the compound.

Endothelin-1 is a powerful long acting, calcium-dependent vasoconstrictor produced by endothelial cells [46]. It is one of three structurally related endothelins but the only one that is vasoactive and produced by endothelial cells [45]. Endothelin-1 is an autacoid and, although small amounts are present in plasma, the peptide acts locally. It is ten times more potent than angiotensin II [46]. Endothelin-1 receptor sites are widely distributed on cells other than vascular smooth muscle, which suggests that the substance has many actions [45]. Renal mesangial vessels are particularly sensitive to the vasoconstriction effects of endothelin-1. Several agonists including thrombin and epinephrine stimulate slow release of endothelin-1 [45].

Cardiopulmonary bypass increases the level of plasma endothelin-1 [73]. The concentration increases progressively from 2.4 pg/mL before bypass to reach a peak of 5.1 pg/mL 4 hours after operation. By 12 hours, the plasma endothelin-1 concentration decreases to nearly prebypass levels [73].

Platelets

Cardiopulmonary bypass directly activates platelets. Activation causes production and release of thromboxane A_2; release of adenosine diphosphate, adenosine triphosphate, calcium, and serotonin from dense storage granules; release of a variety of adhesive, coagulation, and growth regulatory proteins from α-granules; and release of stored lysosomal enzymes [47]. As compared with neutrophils, platelets are a minor source of lysosomal enzymes during CPB [47]. In general, α-granule proteins are not vasoactive, although platelet factor 4 weakly stimulates neutrophil elastase and histamine release from basophils [74]. Adenosine diphosphate is a powerful platelet agonist; adenosine triphosphate is not, and is not vasoactive. Calcium and thromboxane have been discussed above.

Serotonin, 5-hydroxytrytamine, is primarily produced by enterochromaffin cells in the gut and by tryptaminergic neurons in the brain [2]. Platelets do not produce 5-hydroxytryptamine but pick it up during perfusion of intestines. Serotonin released by platelets is an autacoid which generally causes vasoconstriction and helps hemostasis; however, serotonin can also stimulate endothelial cells to produce nitric oxide [45]. 5-Hydroxytryptamine does not alter capillary permeability [2]. Infusions of 5-hydroxytryptamine increase blood pressure, cardiac rate, and contractility. During CPB, the plasma 5-hydroxytryptamine level increases slightly [74] or does not change [51, 52]; measurements show considerable variability [50–52, 74].

White Blood Cells

Cardiopulmonary bypass activates neutrophils by activating complement [34, 35] and also by generating kallikrein [53, 55] from cleavage of prekallikrein during activation of the contact activation system proteins. Kallikrein, C5a, and C3b directly activate neutrophils; platelet activating factor and leukotrienes amplify the process. Cardiopulmonary bypass increases the interleukin-1 level [48] and probably activates monocytes by generating C3b. There is no direct evidence that CPB activates basophils and eosinophils; however, activation of both is likely because C3a and C5a activate basophils and mast cells, and platelet activating factor, histamine, and the chemotactic leukotriene LTB$_4$ activate eosinophils. However, the scarcity of eosinophils renders this concern meaningless.

Activated neutrophils release a variety of vasoactive substances and chemotactic factors that contribute to the whole body inflammatory response. In a "respiratory burst" activated neutrophils produce and release highly cytotoxic reactive oxygen molecules, including hydrogen peroxide, hypobromous and hypochlorous acids, and hydroxyl radicals [56, 57, 75]. Neutrophils produce, store, and release several lysosomal enzymes and various proteases that are cytotoxic even to normal cells. Cardiopulmonary bypass up-regulates the MAC-1 (CD11b/CD18) receptor and causes progressive release of neutrophil elastase, lactoferrin, myeloperoxidase, and markers of reactive oxygen radicals [43, 54, 56, 57, 75]. Loaded with diverse cytotoxic and vasoactive chemicals, activated neutrophils likely mediate much of the inflammatory response to CPB. Evidence indicates that CPB induces activated neutrophils to accumulate in the lungs [35, 58, 59], where they increase vascular permeability and interstitial edema [58].

The level of interleukin-1, which is produced by activated monocytes (macrophages), does not increase during cardiopulmonary bypass but peaks about 24 hours afterward [48]. Interleukin-1 activates helper T cells and mediates many systemic inflammatory responses, including fever, decreased vascular resistance, and increased capillary permeability. Bypass does not affect tumor necrosis factor [48], and there are no data regarding the effect of bypass on interleukin-2, interleukin-6, or lymphokines.

Histamine is a powerful vasoactive autacoid that stimulates specific smooth muscle receptors [2]. Histamine increases capillary permeability and dilates small blood vessels by stimulating H1 and H2 receptors. Histamine is produced primarily by mast cells and basophils and is usually secreted into extracellular fluid. Data regarding plasma histamine in patients during CPB are sparse; in dogs, CPB approximately doubles plasma histamine levels [60]. Protamine given rapidly also may increase plasma histamine levels [61].

As catalogued above, CPB generates a large number of vasoactive materials and cytotoxic chemicals that contribute importantly to the morbidity of open heart operations. Control of the whole body inflammatory response produced by these substances offers an opportunity to reduce morbidity and mortality, and to extend applications of CPB technology. Specific inhibitors are known for many of the vasoactive compounds produced by CPB; however, the multiplicity of compounds and variations in plasma concentrations during and after CPB dictate a massive cocktail of inhibitors if this strategy is to succeed. A preventive strategy is more attractive [62].

Platelets and factor XII are directly activated by contact with synthetic surfaces. All subsequent reactions follow activation of these two blood elements. In vitro, neutrophils are activated by surface contact, but it is not clear that this stimulus is sufficient if activated complement and kallikrein are absent during CPB. Certain prostanoids [63] and disintegrins [76] reversibly inhibit platelets and, within a few minutes of CPB, synthetic surfaces become "passivated" and no longer activate platelets (Shigeta O, Gluszko P, Downing SW, Lu W, Niewiarowski S, Edmunds LH Jr; unpublished results). Thus development of a reversible, tight-binding inhibitor of factor XII offers the prospect of inhibiting many reactions associated with the whole body inflammatory response. Anesthesia, operation, hemodynamic stimuli, heparin, and protamine will still trigger defense and stress reactions, but selective inhibition of factor XII and platelets should attenuate the explosive release of vasoactive material triggered by cardiopulmonary bypass.

Supported by HL 19055 from the National Heart, Lung and Blood Institute.

References

1. Blackstone EH, Kirklin JW, Stewart RW, Chenoweth DE. The damaging effects of cardiopulmonary bypass. In: KK Wu, EC Rossi, eds. Prostaglandins in clinical medicine: cardiovascular and thrombotic disorders. Chicago: Year Book Medical, 1982:355–69.
2. Gilman AG, Rall TW, Nies AS, Taylor P, eds. The pharmacological basis of therapeutics. New York: Pergamon Press, 1990.
3. Clark RE, Beauchamp RA, Magrath RA, Brooks JD, Ferguson TB, Weldon CS. Comparison of bubble and membrane oxygenators in short and long perfusions. J Thorac Cardiovasc Surg 1979;78:655–66.
4. Landymore RW, Murphy DA, Kinley CE, et al. Does pulsatile flow influence the incidence of postoperative hypertension? Ann Thorac Surg 1979;28:261–8.
5. Minami K, Körner MM, Vyska K, Kleesiek K, Knobl H, Körfer R. Effects of pulsatile perfusion on plasmin catecholamine levels and hemodynamics during and after cardiac operations with cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:82–91.
6. Reves JG, Karp RB, Buttner EE, et al. Neuronal and adrenomedullary catecholamine release in response to cardiopulmonary bypass in man. Circulation 1982;66:49–55.
7. Firmin RK, Boulous P, Allen P, Lime RC, Lincoln LCR. Sympathoadrenal function during cardiac operations in infants with the technique of surface cooling, limited cardiopulmonary bypass, and circulatory arrest. J Thorac Cardiovasc Surg 1985;90:729–35.
8. Salerno TA, Henderson M, Kieth MF, Charrette EJP. Hypertension after coronary operation; can it be prevented by pulsatile perfusion? J Thorac Cardiovasc Surg 1981;81:396–9.
9. Kono K, Philibin DM, Coggins CH, et al. Adrenocortical hormone levels during cardiopulmonary bypass with and without pulsatile flow. J Thorac Cardiovasc Surg 1983;85:129–33.
10. Frater RWM, Wakayama S, Oka Y, et al. Pulsatile cardiopulmonary bypass: failure to influence hemodynamics or hormones. Circulation 1980;62(Suppl 1):19–25.
11. Townsend GE, Wynands JE, Whalley DG, Bevan DR. Role of renin-angiotensin system in cardiopulmonary bypass hypertension. Can Anaesth Soc J 1984;31:160–5.
12. Taylor KM, Morton IJ, Brown JJ, Bain WH, Caves PK. Hypertension and the renin-angiotensin system following open-heart surgery. Thorac Cardiovasc Surg 1977;74:840–5.
13. Feddersen K, Delin AK, Haggendal J, Aren C, Radegran K. Effects of cardiopulmonary bypass and prostacyclin on

plasma catecholamines, angiotensin II and arginine-vasopressin. Acta Anaethesiol Scand 1985;29:224–30.

14. Weinstein GS, Zabetakis PM, Clavel A, et al. The renin-angiotensin system is not responsible for hypertension following coronary artery bypass grafting. Ann Thorac Surg 1987;43:74–7.
15. Schaff HV, Mashburn JP, McCarthy PM, Torres EJ, Burnett JC. Natriuresis during and early after cardiopulmonary bypass: relationship to atrial natriuretic factor, aldosterone, and antidiuretic hormone. J Thorac Cardiovasc Surg 1989;98: 979–86.
16. Philbin DM, Levine FH, Emerson CW, Coggins CH, Buckley MJ, Austen WG. Plasma vasopressin levels and urinary flow during cardiopulmonary bypass in patients with valvular heart disease. J Thorac Cardiovasc Surg 1979;78:779–83.
17. Wu W, Zbuzek VK, Bellevue C. Vasopressin release during cardiac operation. J Thorac Cardiovasc Surg 1980;79:83–90.
18. Woods WGA, Forsling ML, Le Quesne LP. Arginine vasopressin, arterial pressure and open heart surgery. Br J Surg 1989;76:29–32.
19. Kharasch ED, Yeo KT, Kenny MA, Amory DW. Influence of hypothermic cardiopulmonary bypass on atrial natriuretic factor levels. Can J Anaesth 1989;36:545–53.
20. Dewar ML, Walsh G, Chiu RC-J, et al. Atrial natriuretic factor: response to cardiac operation. J Thorac Cardiovasc Surg 1988;96:266–70.
21. Pang LM, Stalcup SA, Lipset JS, Hayes CJ, Bowman FO, Mellins RB. Increased circulating bradykinin during hypothermia and cardiopulmonary bypass in children. Circulation 1979;60:1503–7.
22. Ellison N, Behar M, MacVaugh H, Marshall BE. Bradykinin, plasma protein reaction and hypotension. Ann Thorac Surg 1980;29:15–9.
23. Nagaoka H, Yamada T, Hatano R, et al. Clinical significance of bradykinin liberation during cardiopulmonary bypass and its prevention by a kallikrein inhibitor. Jpn J Surg 1975;5: 222–33.
24. DeNayer P. Thyroid hormone action at the cellular level. Hormone Res 1987;26:48–57.
25. Bremner WF, Taylor KM, Baird S, et al. Hypothalamo-pituitary-thyroid axis function during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1978;75:392–9.
26. Holland FW III, Brown PS Jr, Weintraub BD, Clark RE. Cardiopulmonary bypass and thyroid function: a "euthyroid sick syndrome." Ann Thorac Surg 1991;52:46–50.
27. Chu S-H, Huant T-S, Hsu R-B, Wang S-S, Wang C-J. Thyroid hormone changes after cardiovascular surgery and clinical implications. Ann Thorac Surg 1991;52:791–6.
28. Nagaoka H, Innami R, Watanabe M, Satoh M, Murayama F, Funakoshi N. Preservation of pancreatic beta cell function with pulsatile cardiopulmonary bypass. Ann Thorac Surg 1989;48:798–802.
29. Inseri LT, French JH. Magnesium: nature's physiologic calcium blocker. Am Heart J 1984;108:188–93.
30. Swain JA. Endocrine response to cardiopulmonary bypass. In: Utley JR, Ashleigh EA, ed. Pathophysiology and techniques of cardiopulmonary bypass. Baltimore: Williams & Wilkins, 1982:24–33.
31. DaSilav WD, Eiselle JW, Lepow IH. Complement as a mediator of inflammation. J Exp Med 1967;126:1027–48.
32. Gerard C, Hugli TE. Identification of classical anaphylatoxin as the des-Arg form of the C5a molecule: evidence of a modulator role for the oligosaccharide unit in human des-Arg 74-C5a. Proc Natl Acad Sci USA 1981;78:1833–7.
33. Del Balza UH, Levi R, Polley MJ. Cardiac dysfunction caused by purified human C$_3$a anaphylatoxin. Proc Natl Acad Sci USA 1985;82:886–90.
34. Chenoweth DE, Cooper SW, Hugli TE, Stewart RW, Blackstone EH, Kirklin JW. Complement activation during cardiopulmonary bypass. N Engl J Med 1981;304:497–503.
35. Howard RJ, Crain C, Franzini DA, Hood I, Hugli TE. Effects of cardiopulmonary bypass on pulmonary leukostasis and complement activation. Arch Surg 1988;123:1496–501.
36. Kirklin JK, Westaby S, Blackstone EH, Kirklin JW, Chenoweth DE, Pacifico AD. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–57.
37. Hoshikawa-Fujimura AY, Auler JOC Jr, Da Rocha TRF, et al. PAF-acether, superoxide anion and beta-glucuronidase as parameters of polymorphonuclear cell activation associated with cardiac surgery and cardiopulmonary bypass. Braz J Med Biol Res 1989;22:1077–82.
38. Faymonville ME, Deby-Dupont G, Larbuisson R, et al. Prostaglandin E$_2$, prostacyclin and thromboxane changes during non-pulsatile cardiopulmonary bypass in humans. J Thorac Cardiovasc Surg 1986;91:859–66.
39. Ylikorkala O, Saarela E, Viinikka L. Increased prostacyclin and thromboxane production in man during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1981;82:245–7.
40. Davies GC, Sobel M, Salzman EW. Elevated plasma fibrinopeptide A and thromboxane B$_2$ levels during cardiopulmonary bypass. Circulation 1980;61:808–14.
41. Lewis RA, Austen KF, Soberman RJ. Leukotrienes and other products of the 5-lipoxygenase pathway. N Engl J Med 1990;323:645–55.
42. Levi R, Krell RD, eds. Biology of the leukotrienes. New York: Academy of Sciences, 1988:524.
43. Wachtfogel YT, Kucich U, Greenplate J, et al. Human neutrophil degranulation during extracorporeal circulation. Blood 1987;59:324–30.
44. Stibbe J, Kluft C, Brommer EJP, Gomes M, DeJong DS, Nauta J. Enhanced fibrinolytic activity during cardiopulmonary bypass in open-heart surgery in man is caused by extrinsic (tissue-type) plasminogen activator. Eur J Clin Invest 1984; 14:375–82.
45. Vane JR, Anggard EE, Botting RM. Regulatory functions of the vascular endothelium. N Engl J Med 1990;323:27–36.
46. Yanagisawa M, Kurihara H, Kimura S, et al. A novel potent vasoconstrictor peptide produced by vascular endothelial cells. Nature 1988;332:411–5.
47. Addonizio VP Jr, Strauss JF III, Chang L-F, Fisher CA, Colman RW, Edmunds LH Jr. Release of lysosomal hydrolases during simulated extracorporeal circulation. J Thorac Cardiovasc Surg 1982;84:28–34.
48. Haeffner-Cavaillon N, Roussellier N, Ponzio O, et al. Induction of interleukin-1 production in patients undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg 1989;98: 1100–6.
49. Rees DD, Palmer RMJ, Moncada S. Role of endothelium-derived nitric oxide in the regulation of blood pressure. Proc Natl Acad Sci USA 1989;86:3375–8.
50. Feddersen K, Aurell M, Haggendal J, Radegran K. Effects of cardiopulmonary bypass and prostacyclin on plasma catecholamines, angiotensin II, and arginine-vasopressin. Acta Anaesthesiol Scand 1985;29:224–30.
51. Demos MA, Strauss RJ, Schnipper LE, Stuckley JH. Plasma serotonin levels during total cardiopulmonary bypass. J Thorac Cardiovasc Surg 1970;60:257–63.
52. Anger C, Carter JA, Prys-Roberts C. Antihypertensive mechanisms of ketanserin in postoperative hypertension after cardiopulmonary bypass. Anesth Analg 1988;67:99–106.
53. Kongsgaard UE, Smith-Erichson N, Geiran O, Amundsen E, Mollenes TE, Garred P. Different activation patterns in the plasma kallikrein-kinin and complement systems during coronary bypass surgery. Acta Anaesthesiol Scand 1989;33: 343–7.
54. Goldstein RE. Involvement of leukocytes and leukotrienes in ischemic dysfunction of the coronary microcirculation. Eur Heart J 1990;11(Suppl B):16–26.
55. Wachtfogel YT, Harpel PC, Edmunds LH Jr, Colman RW. Formation of C1$_5$-C1-inhibitor, kallikrein-C1-inhibitor and plasmin-alpha 2-plasmin-inhibitor complexes during cardiopulmonary bypass. Blood 1989;73;468–71.
56. Hind CRK, Griffin JF, Latchman YE, et al. Effect of cardiopulmonary bypass on circulating concentrations of leucocyte

elastase and free radical activity. Cardiovasc Res 1988;22: 37–41.

57. Davies SW, Underwood SM, Wickens DG, Feneck RO, Dormandy TL, Walesby RK. Systemic pattern of free radical generation during coronary bypass surgery. Br Heart J 1990; 64:236–40.
58. Craddock PR, Fehr J, Brigham KL, et al. Complement and leukocytes mediate pulmonary dysfunction in hemodialysis. N Engl J Med 1977;296:769–74.
59. Ratcliff NB, Young WG, Hackel DB, Mikat E, Wilson JW. Pulmonary injury secondary to extracorporeal circulation. J Thorac Cardiovasc Surg 1973;65:425–32.
60. Man WK, Brannan JJ, Fessatidis I, Beckett J, Taylor KM. Effect of prostacyclin on the circulatory histamine during cardiopulmonary bypass. Agents Actions 1986;18:182–5.
61. Stoelting RK, Henry DP, Verburg KM, McCammon RL, King RD, Brown JW. Haemodynamic changes and circulating histamine concentrations following protamine administration to patients and dogs. Can Anaesth Soc J 1984;31:534–40.
62. Edmunds LH Jr. The sangreal. J Thorac Cardiovasc Surg 1985;90:1–6.
63. Kappa JR, Fisher CA, Todd B, et al. Intraoperative management of patients with heparin-induced thrombocytopenia. Ann Thorac Surg 1990;49:714–23.
64. Wallach R, Karp RB, Reves JG, Oparil S, Smith LR, James TN. Pathogenesis of paroxysmal hypertension developed during and after coronary bypass surgery: a study of hemodynamic and humoral factors. Am J Cardiol 1980;46:559–65.
65. Philbin DM. Endocrine response to cardiopulmonary bypass. Mount Sinai J Med 1985;57:508–10.
66. Taylor KM, Brannan JJ, Bain WH, Caves PK, Morton IJ. Role of angiotensin II in the development of peripheral vasoconstriction during cardiopulmonary bypass. Cardiovasc Res 1979;13:269–73.
67. Taylor KM, Bain WH, Russel M, Brannan JJ, Morton IJ. Peripheral vascular resistance and angiotensin II levels during pulsatile and non-pulsatile cardiopulmonary bypass. Thorax 1979;34:594–8.
68. Gorin AB, Liebler J. Changes in serum angiotensin-converting enzyme during cardiopulmonary bypass in humans. Am Rev Respir Dis 1986;134:79–84.
69. Lucchesi BR. Cardiac actions of glucagon. Circ Res 1968;22: 777–87.
70. Braquet P, Touqui L, Shen TY, Vargaftig BB. Perspectives in platelet-activating factor research. Pharm Rev 1987;39:97–145.
71. Addonizio VP Jr, Smith JB, Guiod LR, Strauss JF III, Colman RW, Edmunds LH Jr. The relationship between thromboxane synthesis and platelet protein release during simulated extracorporeal circulation. Blood 1979;54:371–6.
72. Faymonville ME, Pincemail J, Duchateau J, et al. Myeloperoxidase and elastase as markers of leukocyte activation during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1991;102:309–17.
73. Hashimoto K, Horikoshi H, Miyamoto H, Suzuki K, Matsui M, Arai T. Mechanisms of organ failure following cardiopulmonary bypass: the role of elastase and vasoactive mediators. J Thorac Cardiovasc Surg (in press).
74. Zucker MB, Katz IR. Platelet factor 4: production, structure and physiologic and immunologic action. Proc Soc Exp Biol Med 1991;198:693–702.
75. Stahl RF, Fisher CA, Kucich U, et al. Effects of simulated extracorporeal circulation on human leukocyte elastase release, superoxide generation, and procoagulant activity. J Thorac Cardiovasc Surg (in press).
76. Musial J, Rucinski B, Williams JA, Stewart GJ, Edmunds LH Jr, Niewiarowski S. Inhibition of platelet adhesion to surfaces of extracorporeal circuit by disintegrins: RGD-continuing peptides from viper venoms. Circulation 1990;82:261–73.

CORRESPONDENCE

Team Approach for Clinical Cardiac Surgery Research

To the Editor:

Recent advances in computer technology have made it possible to compile data about various characteristics of patient populations, such as surgical procedures performed, postoperative management options, and the clinical outcome of patients. As a result, many academic institutions have placed an increased emphasis on clinical research. To take advantage of advances in the areas of computer technology, biostatistics, and data compilation, researchers must have expertise in these specific branches of science. The importance of the coordinated effort of many professionals is central to achieving quality clinical research in academic surgery, particularly in the field of cardiac surgery.

Many factors should be considered when planning data collection and research strategies. These factors include the logistics of data collection, storage, and retrieval, as well as the difficulties associated with complex data analysis, interpretation, and presentation. A comprehensive research plan requires staff with expertise in data collection, data entry, database programming, research design, statistics, and data analysis. Database management has become an efficient means of conducting clinical research; one computer can replace vast filing systems, and electronic data storage can quickly produce multiple reports. Because the task of data collection, analysis, interpretation, presentation, and reporting, when it involves computerized databases, is a complex process, it is important to include experts in research design and statistics as members of the research team. These professionals can help to prevent design flaws that may threaten the validity of the studies. Using the technique of power analysis, they can make critical suggestions on sample size [1], which in many cases may determine whether the findings of the study will achieve statistical significance.

A preferred research team comprises specialized staff for data collection, data entry, database management, microcomputer work, mainframe programming, and research design/statistics. The clinical data collector abstracts data from many complex sources (eg, medical records, patient charts). The data entry expert transfers the abstracted data to the computer. The computer programmer provides software programming to facilitate data entry. The microcomputer expert solves database and data entry problems and converts data into an exchangeable form. The mainframe computer expert is responsible for the conversion of data entered in alphanumeric or database form (eg, yes/no) to purely numeric or research form (eg, 1, 0), the analysis of these data using a variety of statistical methods, and the storage of data. The statistician and research experts must be involved from the beginning of the research project to ensure that potential problems are identified before data collection. They can identify areas where precise data collection will provide a more accurate estimate of clinical impact. The value of sample size analysis before conducting a research study is paramount, and this determination most often falls in the domain of the statistician. Predetermining the sample size is important because insufficient sample size will result in the inability to demonstrate statistical and thus clinical importance. A reduced sample size is beneficial because it may decrease the time and cost involved in a study. The statistician also determines what type of statistical analysis should be applied to the clinical data. Current research designs usually involve repeated measures and multifactorial occurrences. Therefore, complex research designs may require a sophisticated statistical analysis, thus demonstrating the need for an expert who can solve multifactorial problems.

Clinical research in an academic center is helpful for improving patient care, identifying important surgical risk factors, and reducing operative mortality and morbidity. As a result, researchers are taking an increased interest in the easily obtainable data collected at various hospitals at the regional [2], state [3], and national [4] levels. The ideal cardiac surgery research team is a true collaboration of efforts among cardiac surgeons and various experts in database management. This team approach provides a productive scientific atmosphere and enhances the quality of the research work. Thus, a coordinated cardiac surgery research team may increase the academic productivity of an institution where clinical research is an important priority.

Charles C. Canver, MD

Section of Cardiothoracic Surgery
Dartmouth Medical School
Dartmouth-Hitchcock Medical Center
One Medical Center Dr
Lebanon, NH 03756

Roger C. Fiedler, PhD

Department of Surgery
SUNY at Buffalo
100 High St
Buffalo, NY 14203

References

1. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Erlbaum Associates, 1988.
2. O'Connor GT, Plume SK, Olmstead EM, et al. A regional prospective study of in-hospital mortality associated with coronary artery bypass grafting. JAMA 1991;266:803–9.
3. Hannan EL, Kilburn H Jr, O'Donnell JF, Lukacik G, Shields EP. Adult open heart surgery in New York state: an analysis of risk factors and hospital mortality rates. JAMA 1990;264:2768–74.
4. Grover FL, Hammermeister KE, Burchfiel C, Cardiac Surgeons of the Department of Veterans Affairs. Initial report of the Veterans Administration preoperative risk assessment study for cardiac surgery. Ann Thorac Surg 1990;50:12–28.

Length of the In Situ Right Gastroepiploic Artery for Coronary Artery Bypass

To the Editor:

In a recent article, Saito and colleagues [1] described the availability of right gastroepiploic artery (GEA) grafts in terms of length and diameter as examined at the time of operation and angiographically. In a recently published study, we [2] described an anatomical study of the GEA in cadavers to assess the length of this arterial conduit in situ and try to determine the shortest route (antegastric versus retrogastric) to the recipient coronary arteries for its use in coronary revascularization. The length of the conduit was measured from its origin until the point where the internal diameter allowed a 1.5-mm-caliber probe, which is enough to perform an anastomosis. In our study, in all patients the midpoint of all coronary arteries could be reached with an in situ GEA. The length of the harvested GEA conduits varied from 25 to 31 cm (mean, 26.7 ± 1.9 cm). The shortest route to the right main coronary artery, the posterior descending artery, and the circumflex branch was retrogastric and posterior to the left lobe of the liver, whereas to the diagonal branch and the left anterior descending artery the antegastric route was shorter (in 3 patients with hepatomegaly a route posterior to the left lobe of the liver was shorter). However the differences between the antegastric and retrogastric routes were not statistically significant.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:1244–9 • 0003-4975/92/$5.00

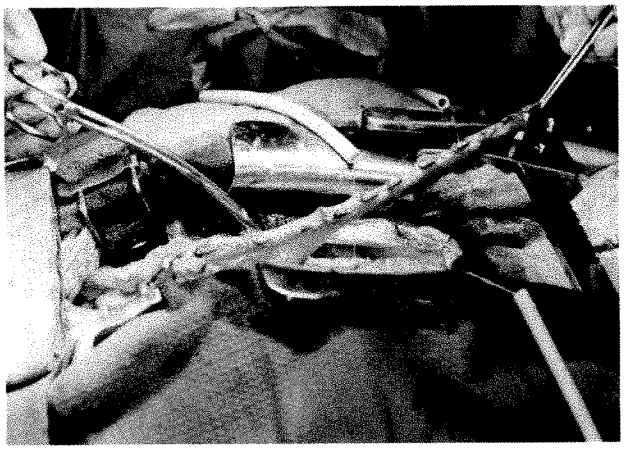


Fig 1. Obtained length of the right gastroepiploic artery pedicle from the abdomen (left) to over the ascending aorta (right).

Our autopsy data confirm the clinical and angiographical findings of Saito and co-workers that with an in situ GEA all coronary arteries could be reached, although we believe that retrogastric routing may be more appropriate for the main right and circumflex arteries and their branches. In our clinical routine we use the retrogastric routing to revascularize the posterior and inferior surface of the heart, although this may be technically more demanding. An advantage of the retrogastric versus antegastric routing is a decreased risk of injury during later laparotomy. A disadvantage of retrogastric routing may be the more difficult control of bleeding, but ligation of the GEA branches instead of stapling can decrease this complication. Finally, we agree that from an anatomical standpoint, preoperative celiac angiography is not necessary as a routine procedure for evaluation of the GEA in coronary revascularization.

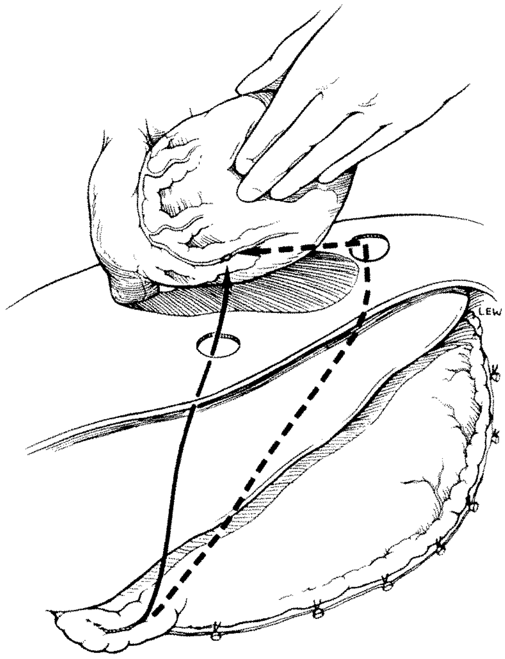


Fig 2. Required length of the in situ right gastroepiploic artery pedicle for the anterior and posterior route at the time of anastomosis. The target coronary artery comes up anteriorly by retraction of the heart upward; the pedicle through the posterior route needs additional length whereas the anterior route does not.

Giuseppe Tavilla, MD

Department of Cardiopulmonary Surgery
Catharina Hospital, PO Box 1350
5602 ZA, Eindhoven
The Netherlands

References

1. Saito T, Suma H, Terada Y, Wanibuchi Y, Fukuda S, Furuta S. Availability of the in situ right gastroepiploic artery for coronary artery bypass. Ann Thorac Surg 1992;53:266–8.
2. Tavilla G, van Son JAM, Verhagen AF, Smedts F. Retrogastric versus antegastric routing and histology of the right gastroepiploic artery. Ann Thorac Surg 1992;53:1057–61.

Reply

To the Editor:

My colleagues and I are grateful for Dr Tavilla's favorable comments on our article [1].

In fact, in situ right gastroepiploic artery (GEA) pedicle is long enough to reach to any part of the coronary artery in the majority of patients (Fig 1). The choice of the intraabdominal route, anterior or posterior to the liver and the stomach, may depend on the surgeon's preference. One practical point that I would like to mention is there is no big difference in the length of the pedicle required at the time of the anastomosis between the anterior and the posterior route.

To get a clear view of the anastomotic site at the time of graft–coronary artery anastomosis, the heart is retracted upward and the distal part of the circumflex or the right coronary artery comes out more anteriorly. In this situation, the pedicle located in the posterior route needs additional length to reach the target site because the hole in the diaphragm was made at a very deep (posterior) site. On the other hand, the pedicle through the anterior route does not require such additional length because the hole is located more anteriorly in the diaphragm (Fig 2).

Thus, the length of the pedicle required to the anastomosis is not significantly different between the anterior and the posterior route unless the anastomosis is performed at the deep site of the pericardial space, placing the heart at a nearly natural position in the posterior route technique.

Again, I thank Dr Tavilla for reconfirming our findings positively.

Hisayoshi Suma, MD

Department of Cardiovascular Surgery
Mitsui Memorial Hospital
1-Izumicho, Kanda, Chiyodaku
Tokyo 101, Japan

Reference

1. Saito T, Suma H, Terada Y, Wanibuchi Y, Fukuda S, Furuta S. Availability of the in situ right gastroepiploic artery for coronary artery bypass. Ann Thorac Surg 1992;53:266–8.

Electrical Instability During Reperfusion

To the Editor:

In their recent article, Kinoshita and associates [1] presented a multivariate analysis of factors associated with ventricular fibrillation during reperfusion after cardioplegia. The phenomenon of reperfusion-induced arrhythmias is complex, and this group of investigators is to be commended for their efforts to improve our understanding of it. I have one observation and one criticism that I would like to share with Dr Kinoshita and associates.

The electrophysiologic recovery of the heart after cardioplegic arrest is currently not well understood. It is influenced by a large number of factors, a few of which were pointed out in Dr Kinoshita's study [1]. Others probably include the *intensity* of the ischemia (a term that includes other features in addition to the *duration* of ischemia); the presence or absence of ventricular scarring or hypertrophy; the completeness of revascularization in ischemic heart disease; and the precise conditions of reperfusion with regard to pressure, flow, and chemical composition of the reperfusate. None of these factors were included in the multivariate analysis. This observation then leads to my one criticism of the study, which is a criticism of data interpretation rather than data acquisition or analysis.

Dr Kinoshita and associates conclude that the severity of cardioplegia-related ischemia-reperfusion injury is *not* related to the occurrence of ventricular fibrillation. I agree that their study did not find a statistically significant association between ischemia-reperfusion injury and ventricular fibrillation after cardioplegia. However, considering the many factors that probably influence reperfusion arrhythmias and this study's relatively small and heterogenous study population, a negative finding is not totally unexpected. When interpreting their data, such absence of proof cannot be construed as proof of absence. Additional research is required to increase our understanding of electrophysiologic recovery after cardioplegia. Moreover, the notion that reperfusion arrhythmias in some way reflect the metabolic and functional recovery of the heart from ischemia-reperfusion injury should not be abandoned based on this one study with negative findings.

William L. Holman, MD

Department of Surgery
University of Alabama at Birmingham
Birmingham, AL 35294

Reference

1. Kinoshita K, Mitani A, Tsuruhara Y, Kanegae Y, Tokunaga K. Analysis of determinants of ventricular fibrillation induced by reperfusion: dissociation between electrical instability and myocardial damage. Ann Thorac Surg 1992;53:999–1005.

Pulmonary Pseudotumor

To the Editor:

In the May 1992 issue of *The Annals of Thoracic Surgery* there was an article titled "Rounded atelectasis: a pulmonary pseudotumor" [1]. In it, initial description of pulmonary pseudotumor was credited to A. Blesovsky in 1966. I would like to remind the reader that in 1965 I reported a case of "twisted lingula" simulating a solitary pulmonary nodule [2].

Hussam A. Fadhli, MD

Thoracic and Cardiovascular Clinic
3749 Lewis Dr
Port Arthur, TX 77642

References

1. Szydlowski GW, Cohn HE, Steiner RM, Edie RN. Rounded atelectasis: a pulmonary pseudotumor. Ann Thorac Surg 1992;53:817–21.
2. Fadhli H, Derrick JR. Twisted lingula: a cause of a solitary pulmonary nodule. Ann Thorac Surg 1965;1:753–4.

Hemolysis After Open Heart Operations

To the Editor:

We read with great interest the article by Okita and colleagues [1], who administered propranolol to treat postoperative hemolysis due to different causes. We wish to report our experience with pentoxifylline (Trental; Hoechst-Roussel, Somerville, NJ) in the treatment of postoperative hemolysis. This drug may be useful in patients in whom propranolol can not be employed for clinical conditions (eg, congestive heart failure, bradycardia, bronchostenosis).

In these patients we used pentoxifylline as a first step and, if the patients' clinical conditions allowed it, propranolol as a secondary step (Figs 1, 2). Pentoxifylline is a hemorrheologic drug that reduces blood viscosity by acting directly on red blood cells. It also reduces platelet aggregation and improves fibrinolytic activity. More malleable red blood cells result; therefore, mechanical resistance is increased while resistance to shearing stress is improved.

A 20-year-old man with minor β-thalassemic anemia was reoperated on for failing mitral and aortic bioprostheses. Two St. Jude mechanical valves were used. One week postoperatively he started showing hemolysis-related symptoms with lactate dehydrogenase (LDH) levels up to 4,821 IU and a plasma free hemoglobin level of 90 mg/dL. Dark urine and a creatinine level of 221 μmol/L (2.5 mg/dL) were also present. The echocardiogram showed reduced ventricular contractility. We started using 400 mg of pentoxifylline three times daily. After 1 week there was a complete regression of symptoms. Lactate dehydrogenase, creatinine, and free hemoglobin levels were back to normal values. Six years after operation the patient is asymptomatic.

A 50-year-old man underwent redo mitral and aortic valve replacement for failing bioprostheses. Two Medtronic-Hall prostheses were employed. Nine days postoperatively, an apical systolic murmur and clinical evidence of hemolysis (LDH, 3,980 IU; plasma free hemoglobin, 72 mg/dL) prompted a transesophageal echocardiogram. Two small mitral and aortic paravalvular leaks were detected and the ventricular contractility was normal. We started with 400 mg of pentoxifylline three times daily, which successfully reduced the hemolysis. The addition of 20 mg of propranolol twice daily completely resolved the hemolysis. Eighteen months postoperatively, the patient is in good clinical condition with no signs of hemolysis.

A 50-year-old man underwent redo aortic and mitral valve

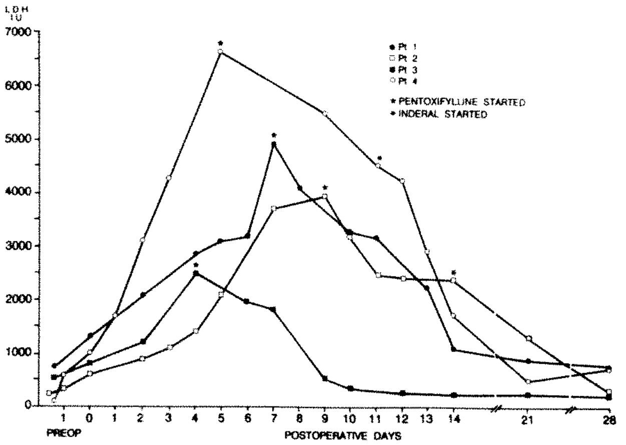


Fig 1. Clinical course of lactate dehydrogenase (LDH) *level.*

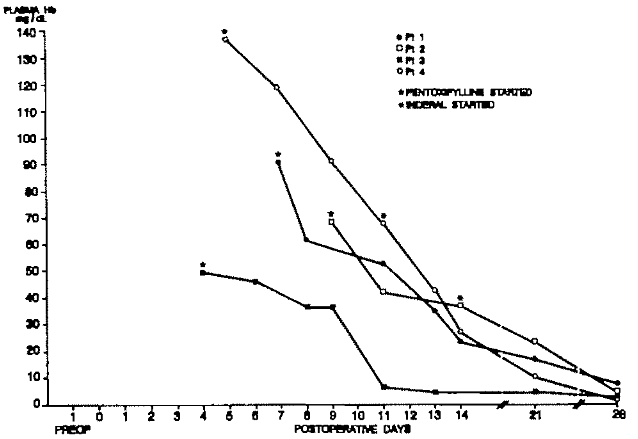


Fig 2. *Clinical course of plasma free hemoglobin (Hb) level.*

replacement for failing bioprostheses. Two Carbomedics prostheses were employed. Again clinical signs of hemolysis with LDH levels up to 2,670 IU and a plasma free hemoglobin level of 53 mg/dL were detected. An echocardiogram showed a small mitral paravalvular leak and borderline ventricular function. The use of 400 mg of pentoxifylline three times daily eliminated the signs of hemolysis. Seven months postoperatively the patient is well.

A 43-year-old man underwent redo mitral and aortic valve replacement for failing bioprostheses, and two Medtronic-Hall valves were used. There was an early onset of hemolysis (LDH, 6,600 IU; plasma free hemoglobin, 135 mg/dL) and the echocardiogram showed a small paravalvular aortic leak with a hypertrophied, well-contracting left ventricle. We started using 400 mg of pentoxifylline three times daily, which reduced the hematological signs of hemolysis (LDH, 2,800 IU; plasma free hemoglobin, 69 mg/dL). The addition of 20 mg of propranolol three times daily completely cured the hemolysis. Six months after operation the patient is asymptomatic.

We think that the use of pentoxifylline can be effective in the treatment of mechanical hemolysis after cardiac operations. If pentoxifylline does not completely correct hemolysis, the use of propranolol should be considered as hemodynamic conditions permit.

Alessandro Golino, MD
Paolo Stassano, MD
Nicola Spampinato, MD

Department of Cardiac Surgery
Second Medical School
University of Naples
5, via S. Pansini
80131 Naples
Italy

Reference

1. Okita Y, Miki S, Kusuhara K, Ueda Y, Tahata T, Yamanaka K. Propranolol for intractable hemolysis after open heart operation. Ann Thorac Surg 1991;52:1158–60.

Reply

To the Editor:

We thank Dr Golino and associates for their comments regarding our article [1]. In their letter, they have drawn attention to an advantage of use of pentoxifylline (Trental) for intravascular hemolysis after prosthetic valve insertion. They reported 4 patients, 3 of whom had signs of paraprosthetic valve leakage. All 4 patients clinically showed a regression of hemolysis after pentoxifylline administration. Additionally, 2 patients received propranolol. None of them underwent reoperation for paraprosthetic valve leakage. However, our experience regarding intravascular hemolysis due to paraprosthetic valve leakage after insertion of St. Jude Medical prostheses [2] was quite different. One of 9 patients died of multiorgan failure and the other 8 patients needed reoperation to repair paraprosthetic leakages. Our 4 patients did receive pentoxifylline for the purpose of alleviating the hemolysis but showed no improvement. One patient showed a transient improvement of hemolysis after propranolol administration as we reported. Although not all patients who have paraprosthetic valve leakage demonstrated severe intravascular hemolysis due to mechanical trauma to erythrocytes, we believe that patients with a small leakage in Dacron-cuffed St. Jude Medical mitral prostheses usually suffer intractable intravascular hemolysis and need reoperation. Propranolol or pentoxifylline sometimes reduces the degree of hemolysis and shortens the period of natural healing of hemolysis. We, however, like to emphasize that such agents never substitute for reparative operation.

Yutaka Okita, MD
Shigehito Miki, MD

Department of Cardiovascular Surgery
Tenri Hospital
200 Mishima, Tenri, Nara
Japan 632

References

1. Okita Y, Miki S, Kusuhara K, Ueda Y, Tahata T, Yamanaka K. Propranolol for intractable hemolysis after open heart operation. Ann Thorac Surg 1991;52:1158–60.
2. Okita Y, Miki S, Kusuhara K, et al. Intractable hemolysis caused by perivalvular leakage following mitral valve replacement with St. Jude Medical prostheses. Ann Thorac Surg 1988;46:89–92.

Penetrating Cardiac Trauma

To the Editor:

We read with interest the article by Knott-Craig and associates [1] and congratulate them on a succinct article with excellent results. We thank them for citing one of our previous publications on the subject [2].

We are compelled, however, to correct Knott-Craig and associates regarding the mortality figures they attributed to our article. As reported in our publication [2], the overall survival from all penetrating cardiac injuries was 53.6% (60 of 112). This included a 20% to 25% survival in patients who were "in extremis" (physiologic index, 15 and 20). In their current article [1], Knott-Craig and associates incorrectly state that our mortality for patients requiring emergency room thoracotomy was "almost 100%." We have consistently obtained a survival of 25% to 30% with emergency room thoracotomy [2–4] even in patients who had no vital signs on admission but who had some sign of life in transit to the hospital.

It is also noteworthy that our reports had dealt with both stab *and* gunshot wounds of the heart. Knott-Craig and associates have included only stab wounds, which are known to have a more favorable prognosis. Because the paper was entitled "Penetrating cardiac trauma . . . ," we wonder why gunshot wounds were excluded.

Finally, Knott-Craig and associates add another descriptive term, "critically unstable," to the already long list of narrative titles used to describe the clinical status of the patients. "Fatal," "moribund," "in extremis," "lifeless," and "agonal" are only a few examples of this listing. As underscored by Trinkle [5], a more objective clinical description of the patients should improve the evaluation of different series in terms of management strategies and their results.

Rao R. Ivatury, MD
Michael Rohman, MD

Department of Surgery
Lincoln Hospital
234 E 149th St
Bronx, NY 10451

References

1. Knott-Craig CJ, Dalton RP, Rossouw GJ, Barnard PM. Penetrating cardiac trauma: management strategy based on 129 surgical emergencies over 2 years. Ann Thorac Surg 1992;53:1006–9.
2. Ivatury RR, Nallathambi MN, Rohman M, Stahl WM. Penetrating cardiac trauma. Quantifying the severity of anatomic and physiologic injury. Ann Surg 1987;205:61–6.
3. Ivatury RR, Shah PM, Ito K, Ramirez-Schon G, Suarez F, Rohman M. Emergency room thoracotomy for the resuscitation of patients with "fatal" penetrating injuries of the heart. Ann Thorac Surg 1981;32:377–85.
4. Ivatury RR, Rohman M, Steichen FM, Gunduz Y, Nallathambi M, Stahl WM. Penetrating cardiac injuries: twenty-year experience. Am Surg 1987;53:310–7.
5. Trinkle JK. Penetrating heart wounds: difficulty in evaluating clinical series [Editorial]. Ann Thorac Surg 1984;38:181–2.

Reply

To the Editor:

My colleagues and I thank Drs Ivatury and Rohman for their kind comments regarding our article, and recognize the important contributions they have made through the years on the same subject.

Their contention with the mortality rates for emergency room thoracotomy relates to our statement that "our results . . . [54% mortality] also compare favorably with the mortality rate in similar reports, which range from almost 100% to 26%." Three references were given [1–3], and the mortality rates in these references are 71%, 92%, and 62%, respectively. Second, the 129 patients described in our article represent a consecutive series without any exclusions, as clearly stated in the article. The fact that there were no gunshot wounds among these patients attests to the patterns and instruments of violence in this community, where gunshot wounds are very uncommon. Finally, we share Ivatury and Rohman's opinion that the variety of terminologies describing patients with penetrating trauma makes comparisons difficult. However, accurate clear clinical descriptions of the patient's condition, as portrayed in our article, separated into easily identifiable groups probably make the interpretation of the data as simple as referring to reference tables as suggested by Ivatury and Rohman.

Christopher J. Knott-Craig, MD

Section of Thoracic and Cardiovascular Surgery
The University of Oklahoma
PO Box 26901
920 Stanton Young Blvd
South Pavilion 4SP 250
Oklahoma City, OK 73190

References

1. Ivatury RR, Nallathambi MN, Rohman M, Stahl WM. Penetrating cardiac trauma. Quantifying the severity of anatomic and physiologic injury. Ann Surg 1987;205:61–6.
2. Moore EE, Moore JB, Galloway AC, Eiseman B. Post-injury thoracotomy in the emergency department: a critical evaluation. Surgery 1979;86:590–8.
3. Attar S, Suter CM, Hankins JR, Sequeira A, McLaughlin JS. Penetrating cardiac injuries. Ann Thorac Surg 1991;51:711–6.

Surgery of Aortic Dissections With GRF Glue

To the Editor:

Stimulated by the excellent results of Bachet and co-workers [1], who introduced gelatin-resorcin-formol glue into the surgery of aortic dissections, we have used the glue since 1991. Our technique is similar to the procedure described by Laas and co-workers [2], and our results are comparable [3, 4]: We used gelatin-resorcin-formol glue in 7 patients with type A dissections and in 5 patients with type B dissections without complications. Teflon felts were never necessary. In all type A dissections a preoperatively diagnosed severe aortic incompetence could be repaired by refixating the valve commissures only. An aortic valve replacement was never necessary.

We recommend some technical details that seem to be advantageous: We do not protect the internal lumen of the aorta during the fixation of the glue with a sponge. Instead we insert a Foley catheter (Blocker catheter) and inflate it up to 50 mL. This method has two advantages: (1) we protect the internal lumen of the aorta, and (2) we apply a constant, very efficient compression on the wall layers, which makes the glue more effective. During the fixation period of the glue, which takes about 5 minutes, a low-flow and low-pressure perfusion is maintained. This helps to avoid air embolism into the carotid arteries, which are not cross-clamped.

After the distal anastomosis is completed, the graft is cross-clamped and the rewarming period begins, while the second anastomosis is performed (Fig 1). This technique reduces the hypothermia period.

Harald E. Zeplin, MD

Department of Thoracic and Cardiovascular Surgery
School of Medicine
Pacelliallee 4
6400 Fulda
Germany

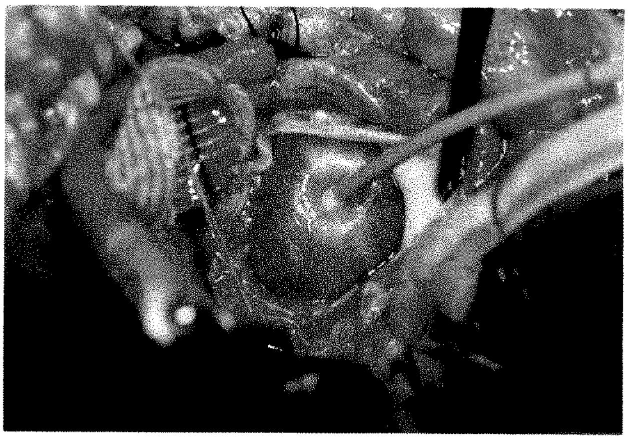


Fig 1. Compression of the aortic wall layers by a Foley catheter after the glue is applied (graft cross-clamped with Crawford clamp).

References

1. Bachet J, Goudot B, Teodori G, et al. Surgery of type A acute dissections with gelatine-resorcine-formol biological glue: a twelve year experience. J Cardiovasc Surg 1990;31:263–73.
2. Laas J, Jurmann MJ, Heinemann M, Borst HG. Advances in aortic arch surgery. Ann Thorac Surg 1992;53:227–32.
3. Zeplin HE, Weingartner J, Berger A, Stegmann TH. Surgical treatment of acute aortic dissections with aid of gelatine resorcine formol glue. Fifth Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery, Alexandria, Egypt, Sep 23–27, 1991, Abstract Volume. Cairo: El Tobgy Press, 1991:233.
4. Zeplin HE, Weingartner J, Stegmann TH. Replacement of the thoracic aorta: improvement of surgical results by use of gelatine resorcin formol glue. J Cardiovasc Surg 1992;33:77–8.

Modified Retractor to Prevent Peripheral Nerve Injury

To the Editor:

I read with interest the correspondence from Dr Briffa and associates [1] in which they describe the disadvantages of a one-stemmed versus a two-stemmed system to retract the sternum for internal mammary artery harvesting.

I would like to share with you our modification of the Ochsner-Favoloro sternal retractor that we have been using for the last 15 years [2]. The modification consists of an angled bar that keeps the stems away from the patient's arm and prevents peripheral nerve injury (Fig 1). Because the distance from the retractor to the sternum has been extended, we also added an extension to the clamps that pull the sternum away (Fig 2). Since we started using this modification about 6 months ago, we have not had any incidents of peripheral nerve injuries. The system can be easily modified at a very low cost.

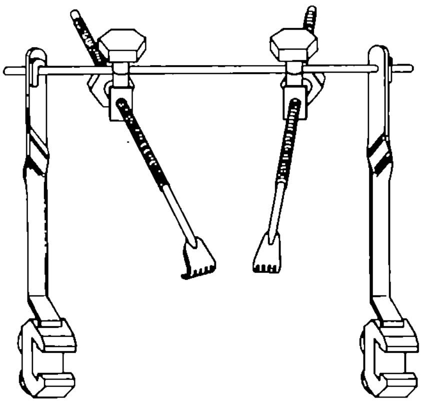


Fig 1. Modification of the Ochsner-Favoloro sternal retractor.

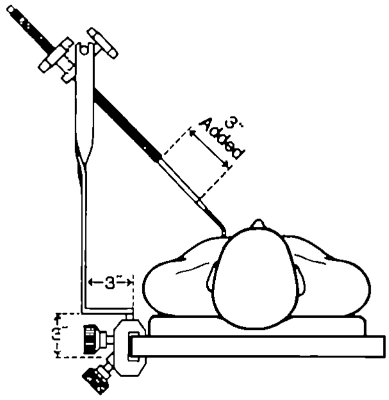


Fig 2. The clamps are extended.

Nelson Ancalmo, MD

Department of Cardiovascular Surgery
Ochsner Clinic of Baton Rouge
16777 Medical Center Dr
Baton Rouge, LA 70816

References

1. Briffa NP, Price C, Grotte GJ, Keenan DJ. Radial nerve injury in patients undergoing coronary artery bypass grafting. Ann Thorac Surg 1992;53:1149–50.
2. Ancalmo N, Ochsner JL. A modified sternal retractor. Ann Thorac Surg 1976;21:174.

THE SOCIETY OF THORACIC SURGEONS

Twenty-ninth Annual Meeting January 25–27, 1993 San Antonio Convention Center, San Antonio, Texas

The Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons will be held at the San Antonio Convention Center on January 25–27, 1993, preceded by the Twenty-sixth Postgraduate Program on Sunday, January 24. The meeting is open to all duly qualified physicians. Both members and nonmembers are urged to register in advance.

The 1992 Program Committee is very pleased with the response to the abstract call, counting 450 abstracts submitted. In addition to the quantity, the high quality of the abstracts made possible the development of a program that represents all aspects of adult and pediatric cardiac surgery and general thoracic surgery. The utilization of breakout sessions continued to be very successful at the last Annual Meeting. On Monday afternoon, there will be parallel Surgical Forums entitled "General Thoracic Research," "Congenital Research," and "Cardiopulmonary Research" running simultaneously from 1:30 to 2:45.

On Tuesday afternoon, all parallel Scientific Sessions will run from 1:30 to 5:00. Session I will include "General Thoracic Surgery I" followed by "General Thoracic Surgery II" segments. Session II will include "Congenital Cardiac Surgery" followed by "Adult Cardiac Surgery," and Session III comprises "Cardiac Assist/Cardiomyoplasty" as well as "Transplantation" segments.

The popular Tuesday morning Problem Case Presentations will be scheduled opposite the Technical "How I Do It" Sessions. The Wednesday morning Clinical Workshops will also continue.

The Committee had an increase in the number of video tapes submitted for the Annual Movie Night, making it possible to develop an excellent program representative of all aspects of the specialty. The movie night session will be in the San Antonio Convention Center.

At 11:35 AM on Tuesday, Dr Richard E. Clark, Chairman of the STS Cardiac Surgery National Database Committee, will provide a status report on the database. He will report on results of the database and recent developments.

New this year, the poster session will feature presentations on general thoracic and cardiovascular subjects. Authors will be present at their posters during Monday and Tuesday breaks to discuss their presentations.

Registration and Fees

An advance registration form with hotel reservation information and details regarding spouses' activities will be mailed to Society members. Nonmembers should write to the Secretary, Richard P. Anderson, MD, The Society of Thoracic Surgeons, 401 N Michigan Ave, Chicago, IL 60611.

Members are not required to pay a registration fee for the Scientific Program. Residents and fellows may register without payment of a registration fee on presentation of a letter from their chief of service. The fee for other physicians is $250, except guest speakers, authors, coauthors, and invited discussants. Nurses and paramedical personnel may register on payment of a $50 fee and presentation of a letter of introduction from a Society member.

The Postgraduate Program is sponsored by the Committee on Postgraduate Education of The Society. Registration fee, which includes lunch, for the Postgraduate Program is $65 for all physicians, residents, and fellows.

There will be no mail-in registration for the concurrent Problem Case Presentations or the Technical "How I Do It" Sessions on Tuesday, January 26, or the Clinical Workshops on Wednesday, January 27. Attendance will be by ticket only, and each seminar is limited to 40 physicians. Tickets can be purchased at The Society's registration desk beginning Saturday, January 23, at 1:30 PM. A continental breakfast is included.

Presentation and Publication

Papers presented at the Scientific Session must be submitted to the Secretary at the time of presentation or may be submitted to the Editor prior to the meeting for possible earlier publication.

Speakers for the Scientific Sessions should limit their presentations to 10 minutes, except for the Monday afternoon Forum Sessions, where all presentations will be 5 minutes. They are requested to meet with the projectionist in the preview room prior to the opening of their session to prepare their slides for presentation.

Those who wish to discuss a paper may write the Secretary prior to the meeting. Discussants from the floor should submit their names to the Moderator at the podium prior to the opening of the session during which the paper is to be presented. Discussants from the floor are limited to 2 minutes; primary discussants are limited to 3 minutes.

Discussants will receive a copy of their remarks shortly after the Annual Meeting. Any delay in the return of the corrected discussion to the Editor will hold up publication of the paper. Timely response of all authors and discussants is, therefore, urged because delays are unfair to those who promptly return their material for publication.

Accreditation

The Society of Thoracic Surgeons is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. One credit hour in Category I of the Physician's Recognition Award of the American Medical Association may be claimed for each hour of participation by the individual physician. The Postgraduate Program is authorized for eight hours of Category I CME credit.

© 1992 by The Society of Thoracic Surgeons

Ann Thorac Surg 1992;54:1250–64 • 0003-4975/92/$5.00

TWENTY-SIXTH POSTGRADUATE PROGRAM THE SOCIETY OF THORACIC SURGEONS

Sunday, January 24, 1993
San Antonio Convention Center, San Antonio, Texas

7:30–12:00 **Morning Session**

7:30 Introduction to the 1993 Postgraduate Course
Jeffrey M. Dunn, Philadelphia, PA, and James K. Kirklin, Birmingham, AL, Co-Chairmen, Committee on Postgraduate Education

I. Mini Symposium: Thoracoscopic Procedures
Moderator: Geoffrey M. Graeber, Morgantown, WV

7:40 Pulmonary
Thomas W. Rice, Cleveland, OH

7:55 Pleural
Thomas M. Daniel, Charlottesville, VA

8:10 Mediastinal
Rodney J. Landreneau, Pittsburgh, PA

8:25 Pericardial
Stephen R. Hazelrigg, Milwaukee, WI

8:40 Esophageal
Paul F. Waters, Los Angeles, CA

8:55 Panel Discussion

II. Mini Symposium: Current Pulmonary Surgical Problems
Moderator: Geoffrey M. Graeber, Morgantown, WV

9:15 Surgical Pulmonary Disease in the Immunosuppressed Patient
Harvey I. Pass, Bethesda, MD

9:35 Surgical Considerations in Pulmonary Tuberculosis and Fungal Disease
Walter L. Barker, Chicago, IL

9:55 Panel Discussion

10:15–11:00 Coffee Break: Visit Exhibits

11:00 **III. C.C.C.E.T.S. Basic Science Lecture****
Introduction
Alexander S. Geha, Cleveland, OH, Chairman, Coordinating Committee for Continuing Education in Thoracic Surgery

Transplantation Immunology and the Cardiothoracic Surgeon
David Sachs*, Harvard Medical School, Boston, MA

12:00–1:30 Luncheon

Luncheon Address: Doing Better or Feeling Worse—The Politics of American Health Care
Floyd D. Loop, Cleveland, OH

1:30–4:45 **Afternoon Session**

IV. Mini Symposium: Decision Making in Cardiac Surgery
Moderator: James K. Kirklin, Birmingham, AL

1:30 Decision Making in Cardioplegia
Andrew S. Wechsler, Richmond, VA

2:00 Decision Making in Valve Surgery: Repair, Replacement, and Prosthetic Choices
D. Craig Miller, Stanford, CA

---

* By Invitation

** Open Session

2:30 Panel Discussion

3:00–3:45 Coffee Break: Visit Exhibits

V. Mini Symposium: Transplantation
Moderator: Jeffrey M. Dunn, Philadelphia, PA

3:45 Lung Transplantation—Which Operation, Where, and Why?
John Wallwork*, Cambridge, England

4:05 Applications of Lung Transplantation in Congenital Heart Disease
Vaughn A. Starnes, Stanford, CA

4:25 Panel Discussion

PROGRAM
TWENTY-NINTH ANNUAL MEETING
THE SOCIETY OF THORACIC SURGEONS

January 25–27, 1993

January 25, 1993 (Monday)
Morning

8:00 Business Meeting (members only)

8:05 Opening Remarks for General Scientific Session

8:15–11:15 **Scientific Session**

1. **J. Maxwell Chamberlain Memorial Paper**

   Preoperative Chemotherapy for Stage IIIa (N2) Non–Small Cell Lung Cancer: The Memorial Sloan-Kettering Experience With 136 Patients
   Nael Martini, Mark M. Kris, Betty J. Flehinger, Richard J. Gralla, Katherine M. Pisters, Manjit S. Bains, Michael E. Burt, Patricia M. McCormack, Valerie W. Rusch, and Robert J. Ginsberg, New York, NY

2. Five-Year Experience With the Maze Procedure for Atrial Fibrillation
   James L. Cox, John P. Boineau, Richard B. Schuessler, Kathryn M. Kater, and Demetrios G. Lappas, St. Louis, MO

3. Paraesophageal Hiatal Hernia: Is an Antireflux Procedure Necessary?
   Warren A. Williamson, F. Henry Ellis, Jr, David M. Shahian, and John M. Streitz, Jr, Burlington, MA

4. Strategy for the Prevention of Stroke in Cardiac Surgical Patients
   Thomas H. Wareing, Victor G. Davila-Roman, Bill B. Daily, Suzan F. Murphy, Benico Barzilai, and Nicholas T. Kouchoukos, St. Louis, MO

5. Cardiac Transplantation in Infants and Children
   Mark W. Turrentine, Kenneth A. Kesler, Randall Caldwell, Robert Darragh, Yousuf Mahomed, and John W. Brown, Indianapolis, IN

6. Reoperations on the Thoracic Aorta: Etiology, Surgical Technique, and Prevention
   Thierry Carrel, Miralem Pasic, Tengis Tkebuchava, Ludwig von Segesser, and Marko I. Turina, Zurich, Switzerland

7. Initial Experience With Video-Assisted Thoracoscopic Lobectomy
   Thomas J. Kirby, Michael J. Mack, Rodney J. Landreneau, and Thomas W. Rice, Cleveland, OH, Dallas, TX, and Pittsburgh, PA

11:15–12:00 **Presidential Address**
And It Happened During Our Lifetime . . .
Vincent L. Gott

---

* By Invitation

Afternoon

Parallel Surgical Forums

1:30–2:45 **Forum I: General Thoracic Research**
Moderators: Joel D. Cooper, St. Louis, MO, and Steven M. Keller, Philadelphia, PA

8. Experimental Barrett's Carcinoma: The Effect of Duodenal-Content Reflux
Manuel Pera, Victor F. Trastek, Herschel A. Carpenter, Pedro L. Fernandez, Antonio Cardesa, and Peter C. Pairolero, Rochester, MN

9. Simultaneous Tracheal and Esophageal pH Monitoring: A New Investigation for Reflux-Associated Asthma
Raymund J. Donnelly, Richard G. Berrisford, Catherine I. A. Jack, Jane A. Tran, and Christopher C. Evans, Liverpool, England

10. Disrupted In Vitro Responses to Nerve Stimulation of Human Circular Smooth Muscle in Barrett's Esophagus
David J. Sugarbaker and William Gardner Richards, Boston, MA

11. Isolated Single-Lung Perfusion With Doxorubicin: Is It Superior to Systemic Administration?
Benny Weksler, Bruce Ng, and Michael E. Burt, New York, NY

12. Reversal of Bronchial Epithelial Cancer in Hamsters
Russell W. Sawyer, William G. Hammond, Raymond L. Teplitz, and John R. Benfield, Sacramento, CA

13. Effects of Insufflation on Hemodynamics During Thoracoscopic Procedures
David R. Jones, Geoffrey M. Graeber, Gerald S. Tanguilig, Gerry Hobbs, and Gordon F. Murray, Morgantown, WV

14. Origin of Right Ventricular Dysfunction After Pulmonary Resection
Carolyn E. Reed, Hugh B. Dorman, and Francis G. Spinale, Charleston, SC

15. Thromboembolism in Patients Undergoing Thoracotomy
Stanley K. Ziomek, Raymond C. Read, H. Gareth Tobler, James E. Harrell, Jr, John C. Gocio, David L. Harshfield, Timothy J. Ranval, Gary Purnell, David R. McFarland, Louis M. Fink, and Robert W. Barnes, Little Rock, AR

1:30–2:45 **Forum II: Congenital Research**
Moderators: Adnan Cobanoglu, Portland, OR, and Frank L. Hanley, San Francisco, CA

16. Pulsatile Reperfusion Improves Cerebral Flow Compared With Nonpulsatile Reperfusion After Circulatory Arrest
Mark P. Anstadt, Mark Tedder, Sanjay S. Hegde, Victor Lin Khian Ha, Anthony Perez-Tamayo, Saleh Abdel-aleem, and James E. Lowe, Durham, NC

17. Cerebral Blood Flow and Metabolism: Comparison of Low-Flow Cardiopulmonary Bypass and Hypothermic Circulatory Arrest
Craig K. Mezrow, Ali M. Sadeghi, Alejandro Gandsas, Otto Dapunt, Howard H. Shiang, Rosario Zappulla, and Randall B. Griepp, New York, NY

18. Myocardial Function Is Normal After Rapid Cooling of the In Vivo Neonatal Heart
Jeffrey S. Heinle, Andrew J. Lodge, James R. Mault, Elizabeth G. Whitaker, and Ross M. Ungerleider, Durham, NC

19. Chronic Alterations in Cardiac Mechanics After Fetal Closed-Heart Surgery
Jeffrey M. Dunn, Satinder Sandu, James L. Hechman, and Pierantonio A. Russo, Philadelphia, PA

20. Fetal Cardiac Bypass: Improved Placental Function With High Flow Rates
John A. Hawkins, Steven M. Clark, and William A. Gay, Jr, Salt Lake City, UT

21. Endothelial Cell Viability in an In Vivo Model of Aortic Valve Allografts
Flavian M. Lupinetti, Thomas T. Tsai, and James M. Kneebone, Ann Arbor, MI

22. Analysis of Airway Function of Experimental Immature Whole-Lung Transplants Versus Mature Lobar Transplants
John A. Kern, Curtis G. Tribble, John G. Zografakis, David C. Cassada, Barry B. K. Chan, and Irving L. Kron, Charlottesville, VA

23. Future of Pediatric Heart Transplantation: In Utero Immunologic Manipulations Produce Tolerance to Experimental Cardiac Allografts
Gary M. Kline, Zhenya Shen, Muhammad Mohiuddin, Vincent Ruggiero, Susan Rostami, and Verdi J. DiSesa, Philadelphia, PA

1:30–2:45 **Forum III: Cardiopulmonary Research**
Moderators: Michael K. Pasque, St. Louis, MO, and Andrew S. Wechsler, Richmond, VA

24. Effect of Inflation on ATP Catabolism and Lactate Production During Normothermic Lung Ischemia
Paul R. J. De Leyn, Hans H. J. Schreinemakers, Dirk E. Van Raemdonck, Kanigula Mubagwa, Willem J. Flameng, and Tony Lerut, Leuven, Belgium

25. Inhibition of Platelet Activation Reduces Serum and Tissue Conjugated Diene Levels in Canine Single-Lung Transplantation
Philip C. Corcoran, Suzanne S. Tse, Nevin M. Katz, Yining Wang, James D. St. Louis, Marie L. Foegh, Ali R. Analouei, and Robert B. Wallace, Washington, DC

26. Effect of Chronic Competitive Flow From a Fully Patent Coronary Artery on Internal Mammary Artery Grafts
Richard S. Zeri, Robert M. Lust, Paul A. Spence, Steven B. Hopson, You Su Sun, Masaki Otaki, Stanley R. Jolly, Prabodh M. Mehta, and W. Randolph Chitwood, Jr, Greenville, NC

27. Triiodothyronine (T_3) Enhances Left Ventricular Contractility After Ischemia Without Affecting Myocardial Adenine Nucleotide Stores
Cornelius M. Dyke, Anwar S. Abd-Elfattah, Mai Ding, Kathy Loesser, Rebecca J. Dignan, Andrew S. Wechsler, and David R. Salter, Richmond, VA

28. Prevention of Acute Regional Ischemia With Endocardial Laser Channels
Osvaldo J. Yano, Mark R. Bielefeld, Valluvan Jeevandavam, Michael R. Treat, Charles C. Marboe, Henry M. Spotnitz, and Craig R. Smith, New York, NY

29. Revascularization for Acute Myocardial Infarction: Superiority of Myocardial Protection With Warm Blood Cardioplegia
W. Stewart Horsley, Joseph Whitlark, J. D. Hall, Pan-Chih, Alice H. Huang, Youngja Park, John P. Gott, and Robert A. Guyton, Atlanta, GA

30. **Thoracic Surgery Directors Association Resident Research Award Paper**
Gross and Microvascular Distribution of Retrograde Cardioplegia in Explanted Human Hearts
Richard N. Gates, Hillel Laks, Davis C. Drinkwater, Jeffrey M. Pearl, Ana Maria Zaragoza, William Lewis, Thomas Sorensen, Elias Kaczer, and Paul A. Chang, Los Angeles, CA

31. Regional Deep Hypothermia of the Spinal Cord Protects Against Ischemic Injury During Thoracic Aortic Cross-Clamping
Richard P. Salzano, Jr, Paul F. Altonji, Lee H. Ellison, James Richter, and Peter Deckers, Hartford, CT

3:30–5:00 Business Meeting (members only)

January 26, 1993 (Tuesday)
Morning

7:00–8:00 **Breakfast Sessions**

No advance registration. Attendance by ticket only and limited to 40 per seminar. Tickets can be purchased at the registration desk beginning Saturday, January 23, at 1:30 PM. Price of ticket covers attendance at seminar and continental breakfast. These sessions run concurrently.

Problem Case Presentations (see pp 1261–3 for program)

Technical Sessions—How I Do It (see p 1263 for program)

8:15–11:30 **Scientific Session**

32. Long-Term Results of Mitral Valve Repair for Mitral Regurgitation Due to Degenerative Disease of the Mitral Valve
Tirone E. David, Susan Armstrong, and Zhao Sun, Toronto, Ontario, Canada

33. A Prospective, Randomized Trial of Retrograde Warm Blood Cardioplegia: Myocardial Benefit and Neurologic Threat
Tomas D. Martin, Joseph M. Craver, John P. Gott, William S. Weintraub, James Ramsay, Christine T. Mora, and Robert A. Guyton, Atlanta, GA

34. Esophagectomy: Comparison of Three Techniques From One Institution With a Residency Training Program
Joe B. Putnam, Jr, Douglas M. Suell, Jr, Marion J. McMurtrey, M. Bernadette Ryan, Garrett Walsh, and Jack A. Roth, Houston, TX

35. Cardiac Allografts From High-Risk Donors: Excellent Clinical Results
Gary Y. Ott, Ray E. Herschberger, Ranae R. Ratkovec, Douglas Norman, Jeffrey D. Hosenpud, and Adnan Cobanoglu, Portland, OR

36. Surgery for Congestive Heart Failure: Coronary Bypass, Transplantation, and Cardiomyoplasty
James A. Magovern, George J. Magovern, Sr, Thomas D. Maher, Jr, Daniel H. Benckart, Sang B. Park, Ignacio Y. Christlieb, and George J. Magovern, Jr, Pittsburgh, PA

37. The Video-Assisted Thoracic Surgery Study Group Data
Stephen R. Hazelrigg, Joseph LoCicero III, Susan Nunchuck, Rodney J. Landreneau, Valerie W. Rusch, Michael Mack, Keith S. Naunheim, Robert McKenna, Robert J. Caccavale, Jemi Olak, and the Video-Assisted Thoracic Surgery Study Group, Milwaukee, WI

38. Pulmonary Resection of Metastatic Hypernephroma
Robert J. Cerfolio, Mark S. Allen, Victor F. Trastek, Claude Deschamps, and Peter C. Pairolero, Rochester, MN

39. Impact of Internal Mammary Artery Grafts on Coronary Artery Bypass Operative Mortality and Morbidity
Frederick L. Grover, Randall Johnson, Guillermo Marshall, Karl E. Hammermeister, and Denver Department of Veterans Affairs Cardiac Surgeons, Denver, CO

11:35–12:00 **Special Presentation**

The STS Cardiac Surgery National Database: A Status Report
Richard E. Clark, Pittsburgh, PA

Afternoon

1:30–5:00 **Parallel Scientific Sessions**
Session I

1:30–2:45 **General Thoracic Surgery I**
Moderators: Thomas W. Rice, Cleveland, OH, and Thomas W. Shields, Chicago, IL

40. Surgical Treatment of Stage IV Esophageal Carcinoma: The Role of Radical Surgery
Tony Lerut, Paul R. J. De Leyn, W. Coosemans, and Dirk E. Van Raemdonck, Leuven, Belgium

41. Esophageal Cancer With Airway Invasion: Resect or Irradiate?
Nasser K. Altorki and David B. Skinner, New York, NY

42. Transhiatal Esophagectomy for Carcinoma of the Esophagus: A 7-Year Review of 135 Consecutive Patients
Wickii T. Vigneswaran, Victor F. Trastek, Mark S. Allen, Claude Deschamps, and Peter C. Pairolero, Rochester, MN

43. Operative Management of Pleural Aspergilloma
Gilbert Massard, Pascal Dumont, Pascal Thomas, Norbert Roeslin, Jean-Marie Wihlm, and Georges Morand, Strasbourg, France

44. Surgical Relief of Acute Airway Obstruction Due to Primary Tuberculosis
Michael G. Worthington, Johan G. Brink, John A. Odell, Juliun Buckels, Mark K. De Groot, and Max Klein, Cape Town, South Africa

3:30–5:00 **General Thoracic Surgery II**
Moderators: Valerie W. Rusch, New York, NY, and Earle W. Wilkins, Jr, Williamstown, MA

45. Management of Idiopathic Stenosis of the Trachea
Hermes C. Grillo, Eugene J. Mark, Douglas J. Mathisen, and John C. Wain, Boston, MA

46. Extended Cervical Mediastinoscopy: Prospective Study of 50 Patients
Luis Lopez, Andres Varela, J. Freixinet, S. Quevedo, J. Lopez Pujol, M. Hussein, and A. Salvatierra, Las Palmas, Spain

47. Differences in Postoperative Pain, Shoulder Function, and Morbidity Between Video-Assisted Thoracic Surgery and Muscle-Sparing Open Thoracotomies
Rodney J. Landreneau, Stephen R. Hazelrigg, Michael J. Mack, Maureen K. Perrino, Susan Nunchuck, Pamela S. Ritter, Jennifer DeFino, Robert D. Dowling, Robert J. Keenan, and Peter F. Ferson, Pittsburgh, PA, Milwaukee, WI, and Dallas, TX

48. Accuracy of Chest Roentgenogram and CT Scan in Lung Metastases and the Implication for the Role of Thoracoscopy
Patricia M. McCormack, Karyn Ginsberg, Manjit S. Bains, Michael E. Burt, Nael Martini, Valerie W. Rusch, and Robert J. Ginsberg, New York, NY

49. Thoracoscopy for the Diagnosis of the Indeterminate Solitary Pulmonary Nodule
Michael J. Mack, Stephen R. Hazelrigg, Rodney J. Landreneau, and Tea E. Acuff, Dallas, TX, Milwaukee, WI, and Pittsburgh, PA

50. Surgical Treatment of Diffuse End-Stage Bilateral Bullous Disease of the Lungs Using Video-Assisted Thoracic Surgery and the Argon Beam Coagulator
Ralph J. Lewis, Robert J. Caccavale, and Glenn E. Sisler, New Brunswick, NJ

1:30–5:00 **Session II**

1:30–2:45 **Congenital Cardiac Surgery**
Moderators: Duke E. Cameron, Baltimore, MD, and Kevin Turley, San Francisco, CA

51. Staged Conversion to Arterial Switch for Late Failure of the Systemic Right Ventricle
Roger B. B. Mee, Andrew Cochrane, and Tom R. Karl, Melbourne, Australia

52. Orthotopic Heart Transplantation in Children With Congenital Heart Disease
Pascal R. Vouhé, Daniel Tamisier, Jerome Le Bidois, Daniel Sidi, Philippe Mauriat, Philippe Pouard, Wassim Khoury, Jean Kachaner, and Francine Leca, Paris, France

53. Comparison of the Hormonal Response After Bidirectional Glenn and Fontan Procedures
Richard D. Mainwaring and John J. Lamberti, San Diego, CA

54. The Restrictive Ventricular Septal Defect: How Small Is Too Small to Close?
Carl L. Backer, Richard C. Winters, Vincent R. Zales, Hiroshi Takami, Alexander J. Muster, D. Woodrow Benson, Jr, and Constantine Mavroudis, Chicago, IL

55. Optimal Acid-Base Strategy for Hypothermic Cardiopulmonary Bypass With Circulatory Arrest
Mitsuru Aoki, Fumikazu Nomura, Michael Stromski, Mikes K. Tsuji, James C. Fackler, Paul R. Hickey, David Holtzman, and Richard A. Jonas, Boston, MA, and Cambridge, MA

3:30–5:00 **Adult Cardiac Surgery**
Moderators: John W. Hammon, Jr, Winston-Salem, NC, and Gerald M. Lawrie, Houston, TX

56. Total Revascularization With T Grafts
Alfred J. Tector, Susan Amundsen, Terence M. Schmahl, David C. Kress, John D. Crouch, and Mohan Peter, Milwaukee, WI

57. Cardiopulmonary Bypass in Patients With Previous Completed Stroke
Arthur C. Beall, Jr, James W. Jones, Gene A. Guinn, and Cesar Nahas, Houston, TX

58. Decrease in the Operative Risk of Reoperative Valve Surgery: Analysis of 772 Patients Operated on Between 1980 and 1992
Lawrence H. Cohn, Sary F. Aranki, Robert J. Rizzo, Kimberly A. Cogswell, Gregory S. Couper, and John J. Collins, Jr, Boston, MA

59. Replacement of the Aortic Valve With an Allograft
Donald B. Doty, Guido Michielon, Wang Nai-dong, Roger C. Millar, and A. Steven Cain, Salt Lake City, UT

60. Assessment of Myocardial Viability in the Ischemic Transplant Candidate: Potential Benefits of Coronary Revascularization
Gilles D. Dreyfus, D. Duboc, A. Blasco, C. Dubois, D. Brodaty, P. De Lentdecker, Jean Bachet, B. Goudot, and D. Guilmet, Suresnes, France

61. Surgical Management of Ventricular Tachycardia
Sara J. Shumway, Eric Johnson, Jolene M. Kriett, and W. Steves Ring, Minneapolis, MN

1:30–5:00 **Session III**

1:30–2:45 **Cardiac Assist/Cardiomyoplasty**
Moderators: Ray C.-J. Chiu, Montreal, Quebec, Canada, and James D. Sink, Philadelphia, PA

62. LVAD Support Impairs RV Contractility But Does Not Alter RV Power Output in Closed-Chest, Conscious Dogs
Marc R. Moon, Luis J. Castro, Abe DeAnda, Yasuko Tomizawa, George T. Daughters, Neil B. Ingels, Geraldine C. Derby, and D. Craig Miller, Stanford, CA

63. Pressure–Volume Loop Analysis of Changes in Cardiac Function in Chronic Cardiomyoplasty
Peter W. Cho, Howard R. Levin, William E. Curtis, Joshua E. Tsitlik, Joseph M. DiNatale, David A. Kass, Timothy J. Gardner, and Michael A. Acker, Baltimore, MD

64. Double Cardiomyoplasty: Long-Term Study in a Canine Model
Gregory A. Thomas, Renato Ruggiero, Hiroshi Niinami, Huiping Lu, Robert L. Hammond, Robert Fietsam, Jr, Hidehiro Nakajima, Hisako Nakajima, and Larry W. Stephenson, Detroit, MI

65. Girdling Effect of Nonstimulated Cardiomyoplasty on Left Ventricular Function
Eli R. Capouya, Richard S. Gerber, Davis C. Drinkwater, Jr, Jeffrey M. Pearl, Jeffrey B. Sack, Alon S. Aharon, Steven W. Barthel, Elias M. Kaczer, Paul Chang, and Hillel Laks, Los Angeles, CA

66. Collateral Blood Flow From Skeletal Muscle to Ischemic Myocardium Is Increased With Chronic Electrical Stimulation
William F. Bailey, Jr, Michael G. Magno, Peter D. Buckman, Fred DiMeo, and John D. Mannion, Philadelphia, PA

3:30–5:00 **Transplantation**
Moderators: James K. Kirklin, Birmingham, AL, and G. Alexander Patterson, St. Louis, MO

67. Chronic Mechanical Circulatory Support: Rehabilitation, Low Morbidity, and Superior Survival After Heart Transplantation
Robert L. Kormos, John M. Armitage, Srinivas Murali, Harvey S. Borovetz, Robert L. Hardesty, and Bartley P. Griffith, Pittsburgh, PA

68. Long-Term Functional Results After Bilateral Lung Transplantation: Heart-Lung or Double-Lung Transplantation
Claire Dromer, Jean-Francois Velly, Jacques Jougon, Eugene M. Baudet, and Louis Couraud, Pessac, France

69. Cytomegalovirus Disease After Heart Transplantation: Is Acyclovir Prophylaxis Indicated?
Charles C. Elkins, William H. Frist, Stephen Dummer, James R. Stewart, Walter H. Merrill, Kelly A. Carden, and Harvey W. Bender, Jr, Nashville, TN

70. Lung Transplantation in Ventilated Patients With Cystic Fibrosis
Gilbert Massard, Hani Shennib, Dominique Metras, Roger Giudicelli, Jean Camboulives, David S. Mulder, Christo I. Tchervenkov, Jean-François Morin, Laurent Viard, Michel Noirclerc, and the Cystic Fibrosis Study Group, Montreal, Quebec, Canada, and Marseille, France

71. Growth Potential of the Transplanted Lung in the Infant Primate
Donald D. Thomas, Thomas A. Sandaert, William R. Anton, Debra R. Jones, J. David Godwin, W. Alan Hodson, and Margaret D. Allen, Seattle, WA

72. Limitation of Ischemic Time by Early Aortic Reperfusion in Cardiac Transplantation
David H. Adams, Ashghar Khaghani, and Magdi H. Yacoub, Harefield, England

7:00 **Reception for Members and Guests**

January 27, 1993 (Wednesday)
Morning

7:00–8:00 **Breakfast Sessions**

No advance registration. Attendance by ticket only and limited to 40 per seminar. Tickets can be purchased at the registration desk beginning Saturday, January 23, at 1:30 PM. Price of ticket covers attendance at seminar and continental breakfast. These sessions run concurrently.

Clinical Workshops (see pp 1263–4 for program)

8:15–12:00 **Scientific Session**

73. Randomized Comparison of Intraoperative Blood Reinfusion Techniques During Coronary Artery Bypass Grafting
Victor A. Ferraris, William R. Berry, and Robert R. Klingman, Albany, NY

74. Preliminary Results With Neoadjuvant Therapy and Resection for Esophageal Carcinoma
James R. Stewart, Steven J. Hoff, John L. Sawyers, Michael J. Murray, Walter H. Merrill, William H. Frist, and David H. Johnson, Nashville, TN

75. Thoracoscopic Esophagectomy: Preliminary Results
Dominique Gossot, P. Fourquier, and M. Celerier, Paris, France

76. Is the Internal Thoracic Artery the Conduit of Choice to Replace a Stenotic Vein Graft?
Daniel Navia, Delos M. Cosgrove III, Bruce W. Lytle, Paul C. Taylor, Patrick M. McCarthy, Robert W. Stewart, and Floyd D. Loop, Cleveland OH

77. Coronary Bypass Surgery in Patients With an Ejection Fraction of 0.20 or Less: Long-Term Follow-up
Steven L. Lansman, Marc J. Cohen, M. Arisan Ergin, Jan D. Galla, and Randall B. Griepp, New York, NY

78. Linear LV Aneurysmectomy Scrutinized by Modern Imaging Techniques: Geometric Normalization Yields Improved Clinical Status
John A. Elefteriades, New Haven, CT

79. Cardiopulmonary Bypass in HIV-Positive Patients: Results in 40 Patients
Alejandro Aris, Jose Luis Pomar, and Emilio Saura, Barcelona, Spain

80. Operative Approaches for Left-Sided Carinoplasty
Masazumi Maeda, Kembu Nakamoto, Hiroshi Katsura, Takahiro Okada, and Noriyuki Tsubota, Kagawa, Japan

81. Pulmonary Arteriovenous Malformations: Therapeutic Options
John D. Puskas, Mark S. Allen, and Douglas J. Mathisen, Boston, MA

82. Early Improvement in Ventricular Function After Aortic Valve Replacement as an Independent Predictor of Long-Term Survival
James J. Morris, Hartzell V. Schaff, Charles J. Mullany, Amita Rastogi, Christopher G. A. McGregor, Richard C. Daly, Robert L. Frye, and Thomas A. Orszulak, Rochester, MN

January 25–26, 1993

Poster Session

New this year, the poster session will feature presentations on a variety of general thoracic and cardiovascular subjects. Authors will be on hand during morning and afternoon breaks both Monday and Tuesday.

1. Fifteen-Year Continual Wound Surveillance Study in Patients After Coronary Artery Bypass
Mark Slaughter, May Olson, James T. Lee, Jr, and Herbert B. Ward, Minneapolis, MN

2. Administration of Prostaglandin E_1 After Lung Transplantation Improves Early Graft Function
   Motoi Aoe, Gregory D. Trachiotis, Kan Okabayashi, Takeo Ojika, Joel D. Cooper, and G. Alexander Patterson, St. Louis, MO
3. Aortic Root Replacement With a Composite Graft: A Twenty-Year Experience
   Jean Bachet, J.-L. Termignon, B. Goudot, G. Dreyfus, A. Piquois, D. Brodaty, C. Dubois, P. Delentdecker, and D. Guilmet, Suresnes, France
4. Cardiopulmonary Bypass Impairs Saccharide Intestinal Transport and Increases Gut Permeability
   S. K. Ohri, I. Bjarnason, V. Pathi, A. Khaghani, B. E. Keogh, I. Menzies, M. H. Yacoub, and Kenneth M. Taylor, London, England
5. Arrhythmogenic Right Ventricular Dysplasia: Surgical Results of Fourteen Patients
   Semih Barlas, Colin J. Hilton, Colin Doig, Janet M. McComb, John P. Bourke, Steve S. Furniss, and Ronnie W. F. Campbell, Newcastle-upon-Tyne, England
6. Comparison of Percutaneous Balloon Valvuloplasty and Open Commissurotomy in 105 Consecutive Patients With Mitral Stenosis
   Donald D. Glower, Jeffrey M. Cohen, J. Kevin Harrison, Thomas M. Bashore, J. Scott Rankin, and David C. Sabiston, Jr, Durham, NC
7. Contracture of the Newborn Myocardium After Prolonged Prearrest Cooling: Is It a Calcium Overload Phenomenon?
   Dominique Shum-Tim, Christo I. Tchervenkov, John O. Lough, and Ray C.-J. Chiu, Montreal, Quebec, Canada
8. Diagnostic Algorithm for Acute Superior Vena Caval Obstruction
   Helmut W. Unruh, Winnipeg, Manitoba, Canada
9. Does Preoperative Irradiation Affect Outcome of Cardiac Surgery?
   Mary J. Boylan, Floyd D. Loop, Bruce W. Lytle, Paul C. Taylor, and Delos M. Cosgrove III, Cleveland, OH
10. Early Surgical Approach to Empyema Thoracis
    Daniel Krellenstein and Viswanadham Pothula, New York, NY
11. Effect of Bilateral Internal Mammary and Epigastric Artery Dissection on Sternal Vascularization
    Michel Carrier, Jean Gregoire, Raymond Cartier, Yves Leclerc, and Conrad L. Pelletier, Montreal, Quebec, Canada
12. Enhanced Preservation of Acutely Ischemic Myocardium With Transseptal Left Ventricular Assist
    James D. Fonger, Yin Zhou, Hiro Matsuura, Gabriel Aldea, Harold Lazar, and Richard Shemin, Boston, MA
13. Expression of Neutrophil and Endothelial Adhesion Molecules During Cardiopulmonary Bypass: Comparison of Bubble and Membrane Oxygenators
    A. Marc Gillinov, Jenny M. Bator, Kenton J. Zehr, J. Mark Redmond, Ronald M. Burch, Chiew Ko, Jerry A. Winkelstein, R. Scott Stuart, William A. Baumgartner, and Duke E. Cameron, Baltimore, MD
14. Extracardiac Lateral Tunnel for Conversion to Fontan Circulation
    John C. Laschinger, Richard E. Ringel, Joel I. Brenner, and Joseph S. McLaughlin, Baltimore, MD
15. Failure of the Hemashield Extension in Right Ventricle–Pulmonary Artery Conduits
    Junjiro Kobayashi, Carl L. Backer, Vincent R. Zales, Susan E. Crawford, Alexander J. Muster, and Constantine Mavroudis, Chicago, IL
16. Five-Year Clinical Experience With Artificial Mitral Valve Chordae
    Claudio Zussa, Elvio Polesel, Uberto Da Col, Carlo Valfre, and Robert W. M. Frater, Treviso, Italy, and Bronx, New York
17. Heat Shock Protects Neonatal Heart Against Hypothermic Global Ischemia
    Fumikazu Normura, Mitsuru Aoki, and John E. Mayer, Jr, Boston, MA
18. Hemodynamic Advantages of Left Atrial Epinephrine Administration After Cardiac Surgery
    David A. Fullerton, John St. Cyr, James Albert, and Frederick Grover, Denver, CO

19. Liberalization of Donor Criteria in Lung and Heart-Lung Transplantation
Sara J. Shumway, Marshall I. Hertz, Michael G. Petty, and R. Morton Bolman III, Minneapolis, MN

20. Mid-Term Results After Bidirectional Cavopulmonary Shunts
John A. Hawkins, Robert E. Shaddy, Ronald W. Day, Jane E. Sturtevant, Garth S. Orsmond, and Edwin C. McGough, Salt Lake City, UT

21. Modified Blalock-Taussig Shunts Using Allograft Saphenous Vein
Gábor Bogáts, Erzsebet Kertesz, Marta Katona, Anna Toszegi, and Gabor S. Kovacs, Szeged, Hungary

22. Multiple Regression Analysis of 234 Cases of Accidental Hypothermia
Beat H. Walpoth, Thomas Locher, Beyhan N. Aslan, Dominik Pfluger, and Ulrich Althaus, Bern, Switzerland

23. Pericardial-Peritoneal Shunt: A Simple Alternative in the Treatment of Malignant Pericardial Effusion
Nan Wang, T. Mogensen, J. R. Feikes, E. E. Vhymeister, and Leonard L. Bailey, Loma Linda, CA

24. Phosphodiesterase Inhibition Targets Postischemic Myocardium
Christopher A. Caldarone, Irvin B. Krukenkamp, Paul G. Burns, Bruce D. Misare, and Sidney Levitsky, Boston, MA

25. The Impact of Pulmonary Hypertension on Clinical Outcome of Single-Lung Transplantation
Ko Bando, Robert D. Dowling, Irvin Paradis, Keith L. Stein, John M. Armitage, Mitchel C. Magee, Ajit Shah, Si M. Pham, Robert L. Hardesty, Henry T. Bahnson, and Bartley P. Griffith, Pittsburgh, PA

26. Risk Factors for Reoperation After Repair of Tetralogy of Fallot
Charles B. Huddleston, Neal Bhattacharya, and Thomas L. Spray, St. Louis, MO

27. Sodium Nitroprusside-Induced Paraplegia During Cross-Clamping of the Thoracic Aorta in a Canine Model
Aurel C. Cernaianu, Anthony J. DelRossi, Andreas Olah, Jonathan H. Cilley, Jr, and Teimuraz Gaprindashvilli, Camden, NJ

28. Stentless, Chordally Supported Quadricusp Mitral Bioprosthesis
Robert W. M. Frater, Kangxiong Liao, Darryl Hoffman, Divyakant Gandhi, Khan Nguyen, and Guangfu Gong, Bronx, NY

29. Surgical Correction of Obstructed Total Anomalous Pulmonary Venous Connection in Newborns With Visceral Heterotaxy Syndromes
Markus K. Heinemann, Kathleen N. Fenton, Frank L. Hanley, and Aldo R. Castaneda, Boston, MA

30. Impact of Three-Field Lymph Node Dissection on Staging in Esophageal Carcinoma
Tony E. Lerut, C. de Gheldere, W. Coosemans, and Dirk E. Van Raemdonck, Leuven, Belgium

31. Role of Needle Biopsy and Thoracoscopy in Evaluation and Management of Pulmonary Lesions
Philip A. Templeton, Mark J. Krasna, Ma Kui, Charles S. White, and Joseph S. McLaughlin, Baltimore, MD

32. Thymectomy for the Myasthenia Gravis Patient: Factors Influencing Outcome
William H. Frist, Walter H. Merrill, James R. Stewart, Christopher B. Doehring, Shanti Thirumalai, Gerald M. Fenichel, and Harvey W. Bender, Jr, Nashville, TN

33. Time-Course Study on the Induction of Myocardial Heat Shock mRNA and Proteins After a Brief Period of Hyperthermic Intervention: Cardioprotective Effects After Ischemia
James D. McCully, David P. Chen, and Sidney Levitsky, Boston, MA

34. Transmyocardial Laser Revascularization of an Acute Myocardial Infarction Improves Contractility and Diminishes Necrosis
Keith A. Horvath, John G. Byrne, and Lawrence H. Cohn, Boston, MA

35. Use of Pleural Tenckhoff Catheter to Palliate Malignant Pleural Effusion
Robert Robinson, David Fullerton, James Albert, Julie Sorenson, and Michael Johnston, Denver, CO

36. Video-Assisted Thoracoscopic Esophageal Myotomy for Achalasia
Richard Inculet and Alan G. Casson, London, Ontario, Canada

37. Video-Assisted Thoracoscopic Pneumonectomy: A Technique With Individual Control of Hilar Structures
Henning A. Gaissert, Hon-Chi Suen, Brian F. Myers, Dean M. Donahue, and John C. Wain, Boston, MA

38. Which Cardioplegic Techniques Prevent Ischemia?
Terrence M. Yau, John S. Ikonomidis, Richard D. Weisel, Donald A. G. Mickle, Nobuhiko Hayashida, and Joan Ivanov, Toronto, Ontario, Canada

January 25, 1993 (Monday evening)

8:00–10:00 **Surgical Motion Pictures**
Moderators: Adnan Cobanoglu, Portland, OR, Timothy J. Gardner, Baltimore, MD, and Thomas W. Shields, Chicago, IL

1. Esophageal Leiomyoma
Thomas W. Rice, Thomas J. Kirby, and Michael V. Sivak, Jr, Cleveland, OH

2. Aortic Valve Replacement With Autologous Pericardium
Carlos M. G. Duran, Ricardo Gallo, Ganga Prabhakar, and Naresh Kumar, Riyadh, Saudi Arabia

3. Ross Procedure
John D. Oswalt, Austin, TX

4. Recognition and Surgical Treatment of Right Pneumonectomy Syndrome
David A. Wyatt and Thomas M. Daniel, Charlottesville, VA

5. Repair of Truncus Arteriosus With Interrupted Aortic Arch: Combined Thoracotomy and Sternotomy Approach
Adnan Cobanoglu, Portland, OR

6. Video-Assisted Endoscopic Pulmonary Lobectomies
Gian Carlo Roviaro, Carlo Rebuffat, and Federico Varoli, Milan, Italy

7. Homograft Reconstruction of the Pulmonary Artery for Calcific Fibrosing Mediastinitis
Daniel L. Miller, Eric S. Edell, and Hartzell V. Schaff, Rochester, MN

8. Transatrial-Transpulmonary Repair of Tetralogy of Fallot
Tom R. Karl and Roger B. B. Mee, Parkville, Victoria, Australia

9. Aortic Arch Replacement for Congenital Aortic Septation and Carotid Stenosis
Stephen Westaby, Oxford, England

10. Elephant Trunk Entrapment After Total Aortic Arch Replacement: Intraoperative Diagnosis and Management
Joachim Laas, Markus K. Heinemann, and Hans G. Borst, Hannover, Germany

January 26, 1993 (Tuesday morning)

7:00–8:00 PROBLEM CASE PRESENTATIONS
(6 Simultaneous Sessions)
Session Committee: Timothy J. Gardner, Baltimore, MD, Victor F. Trastek, Rochester, MN, and Kevin Turley, San Francisco, CA

SEMINAR I
PULMONARY
Discussion Leader: Thomas R. J. Todd, Toronto, Ontario, Canada

1. Spontaneous Chylothorax in a Healthy 15-Year-Old Boy Unresponsive to Medical or Surgical Interventions
Michael Perchinsky, William B. Long, and Jonathan G. Hill, Portland, OR

2. Postpneumonectomy Syndrome With Stridor
   Patricia M. McCormack, New York, NY

3. Combined Coronary Revascularization and Major Pulmonary Resection
   Richard H. Maley, David A. Wyatt, and Robert K. Salley, Lexington, KY

SEMINAR II
MEDIASTINAL
Discussion Leader: Robert J. Ginsberg, New York, NY

4. Respiratory Failure Secondary to Substernal Goiter and Thymoma
   Sibu P. Saha, Anthony G. Rogers, Gary F. Earle, and Mario Matos, Lexington, KY

5. Lung Carcinoma Extending Into the Left Atrium
   Robert B. Lee and Panagiotis N. Symbas, Atlanta, GA

6. Management of Tumors of the Superior Mediastinum: Is There a Role for a Cervical Approach?
   Jerry C. Rosenberg, Detroit, MI

SEMINAR III
CHEST TRAUMA/AORTIC INJURY
Discussion Leader: Gus J. Vlahakes, Boston, MA

7. Blunt Chest Trauma and Mediastinal Widening
   Stephen Z. Turney and Safuh M. A. Attar, Baltimore, MD

8. Aortoesophageal Fistula Resulting From a Traumatic Descending Thoracic Aortic Pseudoaneurysm
   Nan Wang, Steve Sparks, and Leonard L. Bailey, Loma Linda, CA

9. Repair of Traumatic Thoracic Aortic Rupture in the Presence of Abdominal Aortic Injury
   Charles Anene, Victor A. Ferraris, William R. Berry, Benjamin B. Chang, and Robert R. Klingman, Albany, NY

SEMINAR IV
SURGERY FOR ASCENDING AORTIC ANEURYSM
Discussion Leader: David A. Ott, Houston, TX

10. Mycotic Transverse Arch Aneurysm
    Bradford P. Blakeman, Henry J. Sullivan, Alvaro Montoya, and Roque Pifarré, Maywood, IL

11. Rupture of Ascending/Arch Aneurysm Into Pulmonary Artery
    Joseph S. Coselli, Houston, TX

12. Repair of Acute Aortic Dissection Type A After Cesarean Section in the 39th Week of Pregnancy
    Thorsten Wahlers, Aiman Alken, and Joachim Laas, Hannover, Germany

SEMINAR V
TECHNICAL COMPLICATIONS AFTER CARDIAC SURGERY
Discussion Leader: Robert A. Guyton, Atlanta, GA

13. Late Dissection After Aortic Valve Replacement
    Masoud Al-Zeerah, George T. Christakis, Stephen E. Fremes, and Bernard S. Goldman, Toronto, Ontario, Canada

14. Posterior Wall Rupture After Mitral Valve Reoperation
    Shalom Silberman, Masoud Al-Zeerah, George T. Christakis, Stephen E. Fremes, and Bernard S. Goldman, Toronto, Ontario, Canada

15. Ventricular Septal Defect After Coronary Endarterectomy
    Himmet Dajee and Robert Greenfield, Newport Beach, CA

SEMINAR VI
VALVULAR SURGERY/ADULT ECMO
Discussion Leader: Norman A. Silverman, Detroit, MI

16. Homograft Valve Replacement in Carcinoid Heart Disease: The Right Choice?
    Sunil K. Ohri, J. Schofield, C. M. Oakley, and Bruce E. Keogh, London, England

17. Extracorporeal Life Support for the Treatment of Acute Cardiac Rejection
    Sary F. Aranki, Robert J. Rizzo, Gregory S. Couper, Russell D. Stanten, Daniel J. FitzGerald, and Lawrence H. Cohn, Boston, MA

18. Unrecognized Dynamic Subvalvular Left Ventricular Outflow Obstruction After Aortic Valve Replacement
    Glenn W. Laub, Robert Clancy, J. Riebman, S. Muralidharan, Javier Fernandez, Mark S. Adkins, William A. Anderson, and Lynn B. McGrath, Browns Mills, NJ

January 26, 1993 (Tuesday morning)

7:00–8:00 TECHNICAL SESSIONS—HOW I DO IT
(6 Simultaneous Sessions)
Session Committee: Adnan Cobanoglu, Portland, OR, Timothy J. Gardner, Baltimore, MD, and Thomas W. Shields, Chicago, IL

SEMINAR I
PULMONARY AUTOGRAFT FOR AORTIC VALVE REPLACEMENT
Ronald C. Elkins, Oklahoma City, OK

SEMINAR II
MANAGEMENT OF THE SMALL AORTIC ROOT
Adnan Cobanoglu, Portland, OR

SEMINAR III
INFANT LUNG TRANSPLANTATION
Thomas L. Spray, St. Louis, MO

SEMINAR IV
MANAGEMENT OF THE THORACOABDOMINAL ANEURYSM
Joseph S. Coselli, Houston, TX

SEMINAR V
TECHNICAL ASPECTS OF PULMONARY SLEEVE RESECTION
L. Penfield Faber, Chicago, IL

SEMINAR VI
TECHNICAL ASPECTS OF TRANSHIATAL ESOPHAGECTOMY
Mark B. Orringer, Ann Arbor, MI

January 27, 1993 (Wednesday morning)

7:00–8:00 CLINICAL WORKSHOPS
(8 Simultaneous Sessions)
Session Committee: Adnan Cobanoglu, Portland, OR, Ronald C. Elkins, Oklahoma City, OK, and Robert J. Ginsberg, New York, NY

WORKSHOP I
AIDS IN THORACIC DISEASE
Joseph LoCicero III, Boston, MA

WORKSHOP II
ADULT ECMO
Robert H. Bartlett, Ann Arbor, MI

WORKSHOP III
POSTRESECTION SPACE PROBLEMS IN BRONCHOPLEURAL FISTULA
Joseph I. Miller, Jr, Atlanta, GA

WORKSHOP IV
ARTERIAL CONDUITS
Bruce W. Lytle, Cleveland, OH

WORKSHOP V

CORONARY SINUS CARDIOPLEGIA

Gerald D. Buckberg, Los Angeles, CA

WORKSHOP VI

NEW BIOPROSTHETIC VALVES

Robert W. M. Frater, Bronx, NY

WORKSHOP VII

NEWER TECHNIQUES IN CHEST WALL RECONSTRUCTION

Peter C. Pairolero, Rochester, MN

WORKSHOP VIII

NEW DEVELOPMENTS IN CODING FOR REIMBURSEMENT

Sidney Levitsky, Boston, MA, and Jeanne Fitzgerald, Ann Arbor, MI

Author Index
Volume 54 (July–December 1992)

KEY TO ABBREVIATIONS USED FOR ARTICLE CLASSIFICATION

* = Original Article
AN = Announcement
CL = Classics in Thoracic Surgery
CR = Case Report
CP = Correspondence
CT = Collective Review
CV = Current Review
DI = Discussion
ED = Editorial
HW = How to Do It
IC = Invited Commentary
KR = Key References
PA = Presidential Address
RE = Report
RV = Review of Recent Books
TR = Tribute
UP = Update

Aaron BL. *see* Trachiotis, Hafner, & others. 1992;54:898–902*
Abe T. *see* Watanabe, Abe, & others. 1992;54:993–4,HW
Abel JG. *see* Gorenstein, Abel, & Patterson. 1992;54:784–6,CR
Acar C, Jebara VA, Portoghese M, Beyssen B, Pagny JY, Grare P, Chachques JC, Fabiani J-N, Deloche A, Guermonprez JL, Carpentier AF. Revival of the radial artery for coronary artery bypass grafting. 1992;54:652–60*
Acar C. *see* Fernandez, Joyce, & others. 1992;54:440–8,DI
Acar C. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Acar C. *see* Uva, Jebara, & others. 1992;54:89–92*
Acinapura AJ. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR
Acuff TE. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
Acuff TE. *see* Mack, Aronoff, & others. 1992;54:403–9*
Adkins MS. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Adkins MS. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Adoumie R, Serrick C, Giaid A, Shennib H. Early cellular events in the lung allograft. 1992;54:1071–7*
Aguilo R, Llobera M. Manual versus stapled bronchial closure: still controversial. 1992;54:1021,CP
Akimoto H. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*
Akins CW. *see* Creswell, Rosenbloom, & others. 1992;54:11–20,DI
Akins CW. *see* Muehrcke, Daggett, & others. 1992;54:876–83*
Akins CW. *see* Pfister, Zaki, & others. 1992;54:1085–92,DI
Akl E-S. *see* Ridley, Khaghani, & others. 1992;54:333–7*
Al Halees Z. *see* Kumar, Prabhakar, & others. 1992;54:989–90,CR
Alajmo F, Calamai G. High-dose aprotinin in emergency coronary artery bypass after thrombolysis. 1992;54:1022,CP
Albuquerque FC, Krasna MJ, McLaughlin JS. Chronic, traumatic pseudoaneurysm of the ascending aorta. 1992;54:980–2,CR
Aldea GS, Connelly G, Fonger JD, Dobnik D, Shemin RJ. Directed atraumatic coronary sinus cannulation for retrograde cardioplegia administration. 1992;54:789–90,HW
Aldrete V. Surgical management of carcinoid heart disease. 1992;54:598,CP
Al-Fadley F. *see* Kumar, Prabhakar, & others. 1992;54:797–9,HW
Al-Halees Z. *see* Kumar, Prabhakar, & others. 1992;54:797–9,HW
Ali IS. *see* Panos, Ali, & others. 1992;54:1137–8*
Al-Ibrahim K. *see* Raffa, Al-Ibrahim, & others. 1992;54:159–60,CR
Alken A. *see* Hirt, Haverich, & others. 1992;54:676–80*
Allen MS. *see* Miller, Allen, & others. 1992;54:410–4*
Allen MS. *see* Pera, Trastek, & others. 1992;54:199–204*
Al-Nowaiser O. *see* Panos, Ali, & others. 1992;54:1137–8*
Alpert CC. *see* Douville, Kratz, & others. 1992;54:56–61*
Altavilla G. *see* Bortolotti, Calabrò, & others. 1992;54:1219–20,CR
Alvarez JM, Teoh N, Deal CW. Repairing the degenerative anterior mitral leaflet. 1992;54:1229–30,HW
Amato JJ. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75,DI
Anagnostoopoulos CE. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75,DI
Ancalmo N. Modified retractor to prevent peripheral nerve injury. 1992;54:1249,CP
Ancalmo N. Transoral cervical esophagogastrostomy using the EEA stapling device. 1992;54:186,UP
Anderson RH. *see* Ho, Gerlis, & others. 1992;54:264–70*
Anderson RV, Siegman MG, Balaban RS, Ceckler TL, Swain JA. Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest. 1992;54:1126–30*
Anderson RV. *see* Siegman, Anderson, & others. 1992;54:1131–6*
Anderson WA. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Anderson WA. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Angelini GD. *see* Hunter & Angelini. 1992;54:1023,CP
Anstadt MP. *see* Tedder, Anstadt, & others. 1992;54:387–91,CV
Aranki SF. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Ariyan S. *see* Letsou, Hogan, & others. 1992;54:925–31*
Armitage JM, Kormos RL, Morita S, Fung J, Marrone GC, Hardesty RL, Griffith BP, Starzl TE. Clinical trial of FK 506 immunosuppression in adult cardiac transplantation. 1992;54:205–11*
Armitage JM. *see* Griffith, Hardesty, & others. 1992;54:846–51*
Armour JA. *see* Murphy & Armour. 1992;54:502–6*
Armstrong S. *see* David, Armstrong, & Sun. 1992;54:661–8*
Arom KV. *see* Fiore, Naunheim, & others. 1992;54:68–73,DI
Aronoff RJ. *see* Mack, Aronoff, & others. 1992;54:403–9*
Asamura H, Goya T, Naruke T, Tsuchiya R, Kondo H, Suemasu K, Nakatsuka T. Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap. 1992;54:147–9,CR
Asano S. *see* Tamiya, Yamashiro, & others. 1992;54:717–24*
Ascer E. *see* Maughan, Mohan, & others. 1992;54:818–25*
Askari P. *see* Hill, Bruhn, & others. 1992;54:699–704*
Askenasy N. *see* Karck, Vivi, & others. 1992;54:348–51*
Asolati M. *see* Bardini, Bonavina, & others. 1992;54:1165–7*
Attar S. Esophageal perforation. 1992;54:809,CP
Attar S, McLaughlin JS. Pericardial window. Reply. 1992;54:192,CP
Auer JE. *see* Hazelrigg, Auer, & Seifert. 1992;54:528–32*
Austen WG. *see* Muehrcke, Daggett, & others. 1992;54:876–83*
Aziz M. *see* Menasché, Peynet, & others. 1992;54:472–8*
Azzu AA. *see* Lamarra, Azzu, & Kulatilake. 1992;54:361–3,CR

Baeza OR, Majid NK, Conroy DP, Donahoo JS. Combined conventional mechanical and ultrasonic debridement for aortic valvular stenosis. 1992;54:62–7*

July issue, pp 1–192; August issue, pp 193–400; September issue, pp 401–608; October issue, pp 609–816; November issue, pp 817–1024; December issue, pp 1025–1308.

Baeza OR. *see* Fiore, Naunheim, & others. 1992;54:68–73,DI
Bains MS. *see* Burt, Fulton, & others. 1992;54:226–32*
Bains MS. *see* Martini, Burt, & others. 1992;54:460–6*
Baker JW. *see* Cummings, Wyatt, & others. 1992;54:276–8*
Balaban RS. *see* Anderson, Siegman, & others. 1992;54:1126–30*
Balaban RS. *see* Siegman, Anderson, & others. 1992;54:1131–6*
Baldwin JC. *see* Hammond, Franco, & Baldwin. 1992;54:379–80,HW
Baldwin JC. *see* Letsou, Hogan, & others. 1992;54:925–31*
Baldwin RT, Cooley DA. Mechanical support for intraventricular decompression in repair of left ventricular disruption. 1992;54:175–6,HW
Baldwin RT, Klima T, Frazier OH, Lonquist J, Radovancevic B. True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient. 1992;54:978–9,CR
Baldwin RT. *see* Cooley & Baldwin. 1992;54:932–6*
Banchieri C. *see* Hill, Bruhn, & others. 1992;54:699–704*
Banks A. *see* Cohen, Banks, & others. 1992;54:1216–8,CR
Banner NR. *see* Ridley, Khaghani, & others. 1992;54:333–7*
Barber MJ. *see* Kron, Kern, & others. 1992;54:617–20*
Bardini R, Bonavina L, Pavanello M, Asolati M, Peracchia A. Temporary double exclusion of the perforated esophagus using absorbable staples. 1992;54:1165–7*
Bardini R, Segalin A, Ruol A, Pavanello M, Peracchia A. Videothoracoscopic enucleation of esophageal leiomyoma. 1992;54:576–7,HW
Bar-El Y, Lieberman Y, Yellin A. Modified urinary collecting bags for prolonged underwater chest drainage. 1992;54:995–6,HW
Barker L. *see* Phillips, Zeff, & others. 1992;54:908–10*
Barnard CN. *see* Odell, Schurek, & others. 1992;54:283–5*
Barner HB. Combined superior and right lateral left atriotomy with division of the superior vena cava for exposure of the mitral valve. 1992;54:594–5,UP
Barner HB. Allogenic vein as a conduit for coronary artery bypass. 1992;54:817,ED
Barner HB. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Barnoud D. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Barrett PW. *see* Irwin, Bianco, & others. 1992;54:669–75,DI
Barrozo CAM. *see* Panos, Ali, & others. 1992;54:1137–8*
Barzilai B. *see* Hogue, Barzilai, & others. 1992;54:562–3,CR
Bashore TM. *see* Glower, Bashore, & Spritzer. 1992;54:368–70,CR
Bastien O. *see* Girard, Quentin, & others. 1992;54:259–63*
Baudet EM. Profound hypothermia and circulatory arrest. 1992;54:596,CP
Baudet EM. *see* Couraud, Baudet, & others. 1992;54:397,CP
Baumgartner WA. Heterotopic transplantation: is it a viable alternative? 1992;54:401–2,ED
Bavinck JH. *see* Schönberger, Everts, & others. 1992;54:1172–6*
Beall AC Jr. *see* Jones, Izzat, & others. 1992;54:44–9*
Beall AC Jr. *see* McLean, Svensson, & others. 1992;54:894–7*
Beckman CB. *see* Spence, Lust, & others. 1992;54:21–6,DI
Beekman RH. *see* Lupinetti, Pridjian, & others. 1992;54:467–71*
Bégin LR, Sheiner NM. Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty. 1992;54:564–5,CR
Belzer FO. *see* Stringham, Paulsen, & others. 1992;54:852–60*
Benfield JR. Tracheoesophageal fistula after chemotherapy for lymphoma. 1992;54:367,IC
Berger RL. Retrograde disc escape in a Harken mitral valve prosthesis. 1992;54:394,CP
Berger RL. *see* Dzik, Fleisher, & others. 1992;54:1177–81*
Bernal JM, Rabasa JM, Echevarria JR, Revuelta JM. Early structural deterioration with the Mitroflow pericardial xenograft in the mitral position. 1992;54:152–4,CR
Bernal JM, Rabasa JM, Revuelta JM. Rapid transfusion after aortic decannulation. 1992;54:816,CP
Berreklouw E. *see* Schönberger, Everts, & others. 1992;54:1172–6*
Beyssen B. *see* Acar, Jebara, & others. 1992;54:652–60*
Bhayana JN. *see* Armitage, Kormos, & others. 1992;54:205–11,DI
Bianco RW. *see* Irwin, Bianco, & others. 1992;54:669–75*
Bidstrup B. *see* Cosgrove, Heric, & others. 1992;54:1031–8,DI
Biocina B. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Biocina B. *see* Kendall, Ciulli, & others. 1992;54:187,CP
Birnbaum PL, Lichtenstein SV, Noble WH, Guslits BG, Kenney BD, Soutter DI, Panos AL, Dorian P, Newman D. Bronchoenteric fistula from an infected internal cardioverter defibrillator. 1992;54:987–8,CR
Birnbaum PL. *see* Panos, Ali, & others. 1992;54:1137–8*
Blanc P. *see* Girard, Quentin, & others. 1992;54:259–63*
Blanche C. Internal mammary artery to lung parenchyma fistula. Reply. 1992;54:603,CP
Blanc-Jouvan F. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Blessios GA. *see* Heerdt, Pond, & others. 1992;54:959–66*
Blin D. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Blitz A, McLoughlin D, Gross J, Schwartz DS, Fisher JD, Kim SG, Frame R, Brodman RF. Combined maze procedure and septal myectomy in a septuagenarian. 1992;54:364–5,CR
Bloch G. *see* Menasché, Peynet, & others. 1992;54:472–8*
Bodnar E. *see* Casabona, De Paulis, & others. 1992;54:681–5,DI
Bodnar E. *see* Graffigna, Pagani, & others. 1992;54:1093–8,DI
Boglioli LR, Traill TA, Casale AS, Reitz BA, Cameron DE. Surgical treatment of postinfarction ventricular septal defect with aortic stenosis. 1992;54:1209–11,CR
Boley TM. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Bolling SF, Groh MA, Mattson AM, Grinage RA, Gallagher KP. Acadesine (AICA-riboside) improves postischemic cardiac recovery. 1992;54:93–8*
Bolman RM III. *see* Armitage, Kormos, & others. 1992;54:205–11,DI
Bolman RM III. *see* Griffith, Hardesty, & others. 1992;54:846–51,DI
Bolman RM III. *see* Irwin, Bianco, & others. 1992;54:669–75*
Bolooki H. *see* Creswell, Rosenbloom, & others. 1992;54:11–20,DI
Bolooki H. *see* Jones, Izzat, & others. 1992;54:44–9,DI
Bolooki H. *see* Kron, Kern, & others. 1992;54:617–20,DI
Bolton JWR, Mayer JE Jr. Unusual complication of temporary pacing wires in children. 1992;54:769–70,CR
Bonavina L. *see* Bardini, Bonavina, & others. 1992;54:1165–7*
Borioni R, Ciani R, Dato GMA, Garofalo R. Surgical stabilization of the flail chest. 1992;54:397–8,CP
Borkon AM, Failing TL, Piehler JM, Killen DA, Hoskins ML, Reed WA. Risk analysis of operative intervention for failed coronary angioplasty. 1992;54:884–91*
Borman JB. *see* Deviri, Izhar, & others. 1992;54:1018–9,CP
Borst HG. *see* Cosgrove, Heric, & others. 1992;54:1031–8,DI
Borst H-G. *see* Hirt, Haverich, & others. 1992;54:676–80*
Borst HG. *see* Karwande, Renlund, & others. 1992;54:1039–45,DI
Bortolotti U, Calabrò F, Loy M, Fasoli G, Altavilla G, Marchese D. Giant intrapericardial solitary fibrous tumor. 1992;54:1219–20,CR
Bortolotti U, Ius P, Thiene G, Minarini M, Milano A, Valfrè C, Talenti E, Valente M, Mazzucco A. The Meadox-Gabbay pericardial xenograft: failure of the unicusp principle. 1992;54:952–8*
Bos E. *see* Schoof, van Suylen, & Bos. 1992;54:602,CP
Bottone W. *see* Casabona, De Paulis, & others. 1992;54:681–5*
Bouvier H. *see* Girard, Quentin, & others. 1992;54:259–63*
Bove EL. *see* Lupinetti, Pridjian, & others. 1992;54:467–71*
Bove EL. *see* Pridjian, Tacy, & others. 1992;54:355–6,CR

Bowers CM. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Bowman RT. *see* Mack, Aronoff, & others. 1992;54:403–9*
Boyce SW. *see* Pfister, Zaki, & others. 1992;54:1085–92*
Boyd AD. *see* Crawford, Galloway, & others. 1992;54:212–5*
Braimbridge MV. The international cardiothoracic surgeon. 1992;54:193–8*
Brambilla E. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Brand WW III. *see* Warren, Heath, & Brand. 1992;54:240–3*
Brău N, Esposito RA, Simberkoff MS. Cardiac valve replacement in patients infected with the human immunodeficiency virus. 1992;54:552–4,CR
Brecelj A. *see* Rakovec, Brecelj, & Zupan. 1992;54:1203–5,CR
Bredée JJ. *see* Schönberger, Everts, & others. 1992;54:1172–6*
Brenner JI. *see* Laschinger, Ringel, & others. 1992;54:371–3,CR
Brichon PY, Blin D, Perez I, Pison C, Blanc-Jouvan F, Pin I, Barnoud D, Brambilla E, Latreille R. Double-lung transplantation using donor lungs with a right tracheal bronchus. 1992;54:777–8,CR
Brodman RF. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR
Brown DG. *see* McCaughan, Hawley, & others. 1992;54:705–11*
Brown PS Jr. *see* Holland, Brown, & Clark. 1992;54:301–5*
Bruhn PS. *see* Hill, Bruhn, & others. 1992;54:699–704*
Bruneval P. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Buchanan S. *see* Harpole, Feldman, & others. 1992;54:50–5*
Buchanan WP. *see* Kon, Link, & others. 1992;54:39–43*
Buche M, Schroeder E, Devaux P, Louagie YAG, Schoevaerdts J-C. Right internal mammary artery extended with an inferior epigastric artery for circumflex and right coronary bypass. 1992;54:381–3,HW
Buckley MJ. *see* Muehrcke, Daggett, & others. 1992;54:876–83*
Burt M, Fulton M, Wessner-Dunlap S, Karpeh M, Huvos AG, Bains MS, Martini N, McCormack PM, Rusch VW, Ginsberg RJ. Primary bony and cartilaginous sarcomas of chest wall: results of therapy. 1992;54:226–32*
Burt ME. *see* Martini, Burt, & others. 1992;54:460–6*
Burton NA, Phillips WS, Macmanus Q, Lefrak EA. Thermo Cardiosystems left ventricular assist device. Reply. 1992;54:1019–20,CP
Butany J. *see* Hsieh, Mishkel, & others. 1992;54:104–10*

Caccavale RJ. *see* Lewis, Caccavale, & others. 1992;54:421–6*
Caccavale RJ. *see* Lewis, Sisler, & Caccavale. 1992;54:80–3*
Calabrò F. *see* Bortolotti, Calabrò, & others. 1992;54:1219–20,CR
Calamai G. *see* Alajmo & Calamai. 1992;54:1022,CP
Calderon M. *see* Sharma, Calderon, & Ott. 1992;54:137–41*
Callow LB. *see* Lupinetti, Pridjian, & others. 1992;54:467–71*
Cambier P. *see* Cohen, Banks, & others. 1992;54:1216–8,CR
Cameron DE. *see* Boglioli, Traill, & others. 1992;54:1209–11,CR
Cameron DE. *see* Jones, Izzat, & others. 1992;54:44–9,DI
Cameron DE. *see* Warren, Heath, & Brand. 1992;54:240–3,DI
Campagna M. *see* Walley, Keon, & others. 1992;54:111–6*
Campagna M. *see* Walley, Keon, & others. 1992;54:117–23*
Canter CE. *see* Spray, Mallory, & others. 1992;54:216–25*
Canver CC. Preoperative morphologic and physiologic assessment of internal thoracic arteries. 1992;54:1020–1,CP
Canver CC, Fiedler RC. Team approach for clinical cardiac surgery research. 1992;54:1244,CP
Cardoso PFG. *see* Hsieh, Mishkel, & others. 1992;54:104–10*
Carpenter HA. *see* Pera, Trastek, & others. 1992;54:199–204*
Carpentier AF. *see* Acar, Jebara, & others. 1992;54:652–60,DI
Carpentier AF. *see* Acar, Jebara, & others. 1992;54:652–60*
Carpentier AF. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Carpentier AF. *see* Uva, Jebara, & others. 1992;54:89–92*
Carrel T, Linka A, Turina MI. Tricuspid valve obstruction caused by plasmacytoma metastasis. 1992;54:352–4,CR
Carroll F, Kramer MD, Acinapura AJ, Tietjen PA, Wagner I, Oiseth S, Smith F. Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia. 1992;54:1212–3,CR
Cartier R. *see* Stringham, Paulsen, & others. 1992;54:852–60,DI
Casabona R, De Paulis R, Zattera GF, di Summa M, Bottone W, Stacchino C, Vrandecic MOP, Morea M. Stentless porcine and pericardial valve in aortic position. 1992;54:681–5*
Casale AS. *see* Boglioli, Traill, & others. 1992;54:1209–11,CR
Castaneda AR. *see* Kern, Jonas, & others. 1992;54:749–54*
Castillo WM. *see* Landreneau, Dowling, & others. 1992;54:142–4,CR
Ceckler TL. *see* Anderson, Siegman, & others. 1992;54:1126–30*
Ceckler TL. *see* Siegman, Anderson, & others. 1992;54:1131–6*
Ceithaml EL. *see* Ungerleider, Greeley, & others. 1992;54:691–8,DI
Ceithaml EL. *see* Vouhé, Tamisier, & others. 1992;54:621–7,DI
Chachques JC. *see* Acar, Jebara, & others. 1992;54:652–60*
Chambers JS. Better salvage in non–small cell lung cancer. 1992;54:399–400,CP
Chambers JS. *see* Crawford, Galloway, & others. 1992;54:212–5,DI
Chambers JS. *see* Martini, Burt, & others. 1992;54:460–6,DI
Chandra AS. *see* Satyanarayana, Rao, & others. 1992;54:810,CP
Chang PA. *see* Pearl, Laks, & others. 1992;54:1144–50*
Chard RB. *see* Larbalestier, Chard, & Cohn. 1992;54:1186–8*
Chaudhuri PK. *see* Pellegrini, Mucci, & others. 1992;54:578–9,HW
Chauhan A. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Chauvaud S. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Chauvaud S. *see* Uva, Jebara, & others. 1992;54:89–92*
Chaux A. *see* Casabona, De Paulis, & others. 1992;54:681–5,DI
Chechani V, Landreneau RJ, Shaikh SS. Open lung biopsy for diffuse infiltrative lung disease. 1992;54:296–300*
Chen C. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Chen C. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Chen E. *see* Christakis, Koch, & others. 1992;54:449–59*
Cheng TO. Ischemic mitral valve repair. 1992;54:190–1,CP
Chipman CW. *see* Ziomek, Harrell, & others. 1992;54:861–8*
Chitwood WR Jr. Clarence Crafoord and the first successful resection of a cardiac myxoma. 1992;54:997–8,CL
Chitwood WR Jr, Cosgrove DM III, Lust RM, Titrator Multicenter Study Group. Multicenter trial of automated nitroprusside infusion for postoperative hypertension. 1992;54:517–22*
Chitwood WR Jr. *see* Spence, Lust, & others. 1992;54:21–6*
Chiu I-S. *see* Leu, Chiu, & others. 1992;54:134–6*
Chiu RC-J. Dynamic cardiomyoplasty. 1992;54:592–3,KR
Chopra PS. *see* Rao & Chopra. 1992;54:600–2,CP
Christakis GT, Koch JP, Deemar KA, Fremes SE, Sinclair L, Chen E, Salerno TA, Goldman BS, Lichtenstein SV. A randomized study of the systemic effects of warm heart surgery. 1992;54:449–59*
Christlieb IY. *see* Furnary, Magovern, & others. 1992;54:1139–43*
Chung H-N. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR
Ciani R. *see* Borioni, Ciani, & others. 1992;54:397–8,CP
Ciavarella D. *see* Dzik, Fleisher, & others. 1992;54:1177–81*
Cimochowski GE. *see* Christakis, Koch, & others. 1992;54:449–59,DI
Citak M, Rees A, Mavroudis C. Surgical management of infective endocarditis in children. 1992;54:755–60*
Ciulli F. *see* Kendall, Ciulli, & others. 1992;54:187,CP
Clack R. *see* Irwin, Bianco, & others. 1992;54:669–75*
Clancy R. *see* Laub, Muralidharan, & others. 1992;54:826–31*

Clark RE. *see* Borkon, Failing, & others. 1992;54:884–91,DI
Clark RE. *see* Douville, Kratz, & others. 1992;54:56–61,DI
Clark RE. *see* Holland, Brown, & Clark. 1992;54:301–5*
Clark RE. *see* Jones, Izzat, & others. 1992;54:44–9,DI
Clark RE. *see* Mitchell, DeBoer, & others. 1992;54:712–6*
Clark RE. *see* Siegman, Anderson, & others. 1992;54:1131–6*
Clerc F. *see* Couraud, Baudet, & others. 1992;54:397,CP
Cobanoglu A. *see* Karwande, Ensley, & others. 1992;54:840–5,DI
Cobanoglu A. *see* Lupinetti, Pridjian, & others. 1992;54:467–71,DI
Cobanoglu A. *see* Stringham, Paulsen, & others. 1992;54:852–60,DI
Cobanoglu A. *see* Vouhé, Tamisier, & others. 1992;54:621–7,DI
Codd JE. *see* Watanabe, Fuse, & others. 1992;54:479–84,DI
Cohen AJ, Banks A, Cambier P, Edwards FH. Post-atherectomy coronary artery aneurysm. 1992;54:1216–8,CR
Cohen SE. *see* Hill, Bruhn, & others. 1992;54:699–704*
Cohn LH. *see* Larbalestier, Chard, & Cohn. 1992;54:1186–8*
Cohn LH. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Collins JJ Jr. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Coltharp WA. *see* Acar, Jebara, & others. 1992;54:652–60,DI
Commerford PJ. *see* Odell, Schurek, & others. 1992;54:283–5*
Conant P. *see* McKeown, Conant, & Hubbell. 1992;54:490–2*
Connelly G. *see* Aldea, Connelly, & others. 1992;54:789–90,HW
Conroy DP. *see* Baeza, Majid, & others. 1992;54:62–7*
Cook WA. *see* Pogrebniak, Haas, & others. 1992;54:33–8,DI
Cooley DA, Baldwin RT. Technique of open distal anastomosis for repair of descending thoracic aortic aneurysms. 1992;54:932–6*
Cooley DA. *see* Baldwin & Cooley. 1992;54:175–6,HW
Cooley DA. *see* Fernandes, Kadivar, & others. 1992;54:732–40*
Cooley DA. *see* Svensson, Crawford, & others. 1992;54:427–39,DI
Cooper JD. *see* Armitage, Kormos, & others. 1992;54:205–11,DI
Cooper JD. *see* Haydock, Low, & others. 1992;54:1189–92*
Cooper JD. *see* Hsieh, Mishkel, & others. 1992;54:104–10*
Cooper JD. *see* Mathisen & Grillo. 1992;54:1053–8,DI
Cooper JD. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP
Cordell AR. *see* Kon, Link, & others. 1992;54:39–43*
Corso PJ. *see* Pfister, Zaki, & others. 1992;54:1085–92*
Coselli JS. *see* Rizzo, Whittemore, & others. 1992;54:1099–109,DI
Coselli JS. *see* Svensson, Crawford, & others. 1992;54:427–39*
Cosgrove DM III. Aortic valve repair. 1992;54:1014–5,KR
Cosgrove DM III. Long-term follow-up results after reconstruction of the mitral valve by leaflet advancement. 1992;54:274–5,IC
Cosgrove DM III, Heric B, Lytle BW, Taylor PC, Novoa R, Golding LAR, Stewart RW, McCarthy PM, Loop FD. Aprotinin therapy for reoperative myocardial revascularization: a placebo-controlled study. 1992;54:1031–8*
Cosgrove DM III. *see* Chitwood, Cosgrove, & others. 1992;54:517–22*
Cosgrove DM III. *see* Golding, Crouch, & others. 1992;54:1059–64*
Cosgrove DM III. *see* Rosenkranz, Murphy, & Cosgrove. 1992;54:779–81,CR
Coughlin TR Jr. *see* Pfister, Zaki, & others. 1992;54:1085–92*
Couper GS. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Couraud L, Baudet EM, Martigne C, Roques XF, Velly J-F, Laborde N, Dubrez J, Clerc F, Dromer C, Vallieres E. Role of the bronchial arteries in lung function. Reply. 1992;54:397,CP
Couraud L. *see* Nashef, Dromer, & others. 1992;54:937–40*
Cox JL. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Cox JL. *see* Hogue, Barzilai, & others. 1992;54:562–3,CR
Crawford BK, Galloway AC, Boyd AD, Spencer FC. Treatment of AIDS-related bronchopleural fistula by pleurectomy. 1992;54:212–5*
Crawford ES. *see* Svensson, Crawford, & others. 1992;54:427–39*
Crawford ES. *see* Svensson, Crawford, & others. 1992;54:74–9*
Crawford FA Jr. *see* Douville, Kratz, & others. 1992;54:56–61*
Crawford FA Jr. *see* Furnary, Magovern, & others. 1992;54:233–9,DI
Crawford FA. *see* Kratz, Gillette, & others. 1992;54:485–9*
Creswell LL, Rosenbloom M, Cox JL, Ferguson TB Sr, Kouchoukos NT, Spray TL, Pasque MK, Ferguson TB Jr, Wareing TH, Huddleston CB. Intraaortic balloon counterpulsation: patterns of usage and outcome in cardiac surgery patients. 1992;54:11–20*
Crittenden MD. *see* Mitchell, DeBoer, & others. 1992;54:712–6*
Crossman D. *see* Efstratiadis, Munsch, & others. 1992;54:1022–3,CP
Crouch RD. *see* Golding, Crouch, & others. 1992;54:1059–64*
Crowley DC. *see* Lupinetti, Pridjian, & others. 1992;54:467–71*
Cruz J. *see* Feindel, Sandhu, & others. 1992;54:1120–5*
Cummings SP, Wyatt DA, Baker JW, Flanagan TL, Spotnitz WD, Rodgers BM, Kron IL, Tribble CG. Successful treatment of postoperative chylothorax using an external pleuroperitoneal shunt. 1992;54:276–8*
Cunningham JM, Gharavi MA, Fardin R, Meek RA. Considerations in the skeletonization technique of internal thoracic artery dissection. 1992;54:947–51*
Cunningham JN Jr. *see* Maughan, Mohan, & others. 1992;54:818–25*
Curtis JJ. *see* Golding, Crouch, & others. 1992;54:1059–64,DI
Curtis JJ. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Curzan M. *see* Pearl, Laks, & others. 1992;54:1144–50*
Cutilletta AF. *see* Wilson, Ilbawi, & others. 1992;54:892–3*
Cybulsky IJ, Lanza LA, Ryan MB, Putnam JB Jr, McMurtrey MM, Roth JA. Prognostic significance of computed tomography in resected N2 lung cancer. 1992;54:533–7*
Cystic Fibrosis Transplant Study Group. *see* Shennib, Noirclerc, & others. 1992;54:27–32*

Daggett WM Jr. *see* Muehrcke, Daggett, & others. 1992;54:876–83*
Daicoff GR. *see* Kratz, Gillette, & others. 1992;54:485–9,DI
Damiani P. *see* Maughan, Mohan, & others. 1992;54:818–25*
Daniel TM, Fleischer KJ, Flanagan TL, Tribble CG, Kron IL. Transhiatal esophagectomy: a safe alternative for selected patients. 1992;54:686–90*
Daniel TM. *see* Mathisen & Grillo. 1992;54:1053–8,DI
Dark JH. *see* Griffin & Dark. 1992;54:1023–4,CP
Dartevelle P. *see* Icard, Regnard, & others. 1992;54:99–103*
Date K. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW
Dato GMA. *see* Borioni, Ciani, & others. 1992;54:397–8,CP
Dauber JH. *see* Griffith, Hardesty, & others. 1992;54:846–51*
David TE. Simplified correction of outflow obstruction after mitral valve replacement. 1992;54:986,IC
David TE, Armstrong S, Sun Z. Clinical and hemodynamic assessment of the Hancock II bioprosthesis. 1992;54:661–8*
David TE. *see* Graffigna, Pagani, & others. 1992;54:1093–8,DI
Davies GG, Wells DG, Sadler R, Mabee TM, Ruffcorn M, Dooley JB. Plateletpheresis and transfusion practice in heart operations. 1992;54:1020,CP
Davis BB. Surgical management of carcinoid heart disease. Reply. 1992;54:598,CP
Davis JT. *see* Ziomek, Harrell, & others. 1992;54:861–8,DI
de Leval MR. Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis. 1992;54:526–7,IC

de Leval MR. *see* Pawade, de Leval, & others. 1992;54:967–70*
De Leyn PRJ. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP
de Napoli S. *see* Icard, Regnard, & others. 1992;54:99–103*
De Paulis R. *see* Casabona, De Paulis, & others. 1992;54:681–5*
Deal CW. *see* Alvarez, Teoh, & Deal. 1992;54:1229–30,HW
DeBakey ME. *see* Svensson, Crawford, & others. 1992;54:74–9*
DeBoer DA. *see* Mitchell, DeBoer, & others. 1992;54:712–6*
Deemar KA. *see* Christakis, Koch, & others. 1992;54:449–59*
Defraigne J-O, Vahdat O, Lavigne J-P, Demoulin J-C, Limet R. Aneurysm of the ascending aorta after cardiac transplantation. 1992;54:983–4,CR
DeLeon SY. *see* Wilson, Ilbawi, & others. 1992;54:892–3*
Deloche A. *see* Acar, Jebara, & others. 1992;54:652–60*
Deloche A. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Deloche A. *see* Uva, Jebara, & others. 1992;54:89–92*
DeMeester TR. *see* Topart, Deschamps, & others. 1992;54:1046–52,DI
Demmy TL, Magovern GJ, Kao RL. Isolated biventricular working rat heart preparation. 1992;54:915–20*
Demoulin J-C. *see* Defraigne, Vahdat, & others. 1992;54:983–4,CR
Derom F. *see* Laub, Muralidharan, & others. 1992;54:826–31,DI
Dervanian P. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Dervanian P. *see* Uva, Jebara, & others. 1992;54:89–92*
Deschamps C. *see* Miller, Allen, & others. 1992;54:410–4*
Deschamps C. *see* Pera, Trastek, & others. 1992;54:199–204*
Deschamps C. *see* Topart, Deschamps, & others. 1992;54:1046–52*
Devaux P. *see* Buche, Schroeder, & others. 1992;54:381–3,HW
Deviri E, Izhar U, Drenger B, Glick Y, Borman JB. Aprotinin treatment during open heart operation in a patient with severe thrombocytopenia. 1992;54:1018–9,CP
Dewar ML. *see* Letsou, Hogan, & others. 1992;54:925–31*
de la Rivière AB. *see* van Heurn, Hamerlijnch, & others. 1992;54:157–8,CR
di Summa M. *see* Casabona, De Paulis, & others. 1992;54:681–5*
Dieter RA Jr. *see* Mathisen & Grillo. 1992;54:1053–8,DI
Dieter RA Jr. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Dietl CA, Torres AR. Simple method to monitor pulmonary artery pressure in infants after cardiac operations. 1992;54:580–1,HW
DiMarco JP. *see* Kron, Kern, & others. 1992;54:617–20*
Dimitri WR, Reid AW. Coronary bypass graft aneurysm. 1992;54:395,CP
Ding W-X. *see* Liu, Su, & Ding. 1992;54:1196–202*
Dobnik D. *see* Aldea, Connelly, & others. 1992;54:789–90,HW
Doi O. *see* Kodama, Doi, & others. 1992;54:1193–5*
Donahoo JS. *see* Baeza, Majid, & others. 1992;54:62–7*
Donaldson MC. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Dooley JB. *see* Davies, Wells, & others. 1992;54:1020,CP
D'Orazio S. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Dorian P. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Doty DB. *see* Karwande, Ensley, & others. 1992;54:840–5*
Douthit MB. *see* Mack, Aronoff, & others. 1992;54:403–9*
Douville EC, Kratz JM, Spinale FG, Crawford FA Jr, Alpert CC, Pearce A. Retrograde versus antegrade cardioplegia: impact on right ventricular function. 1992;54:56–61*
Dowling RD. *see* Landreneau, Dowling, & others. 1992;54:142–4,CR
Dowling RD. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Dowling RD. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
Downar E. *see* Mickleborough, Mizuno, & others. 1992;54:832–9*
Downes TR. *see* Kon, Link, & others. 1992;54:39–43*
Downing SW, Edmunds LH Jr. Release of vasoactive substances during cardiopulmonary bypass. 1992;54:1236–43,CV
Drakeley MJ. *see* Sharpe, Sendegeya, & others. 1992;54:366–7,CR
Drenger B. *see* Deviri, Izhar, & others. 1992;54:1018–9,CP
Dreyfus G. Total orthotopic heart transplantation: an alternative to the standard technique. Reply. 1992;54:187–8,CP
Drinkwater DC. *see* Pearl, Laks, & others. 1992;54:1144–50*
Dromer C. *see* Couraud, Baudet, & others. 1992;54:397,CP
Dromer C. *see* Nashef, Dromer, & others. 1992;54:937–40*
Dubrez J. *see* Couraud, Baudet, & others. 1992;54:397,CP
Dumon J-F. *see* Shennib, Noirclerc, & others. 1992;54:27–32*
Dumont P. *see* Massard, Roeslin, & others. 1992;54:1159–64*
Duncan S. *see* Griffith, Hardesty, & others. 1992;54:846–51*
Dunn SC. *see* Hsieh, Mishkel, & others. 1992;54:104–10*
Dunning JJ, Kendall SWH, Mullins PA, Chauhan A, Graham TR, Biocina B, Schofield PM, Large SR. Coronary artery bypass grafting nine years after cardiac transplantation. 1992;54:571–2,CR
Dunning JJ. *see* Kendall, Ciulli, & others. 1992;54:187,CP
Duran CMG. *see* Fernandez, Joyce, & others. 1992;54:440–8,DI
Duran CMG. *see* Kumar, Prabhakar, & others. 1992;54:797–9,HW
Duran CMG. *see* Kumar, Prabhakar, & others. 1992;54:989–90,CR
Duranceau A. *see* Topart, Deschamps, & others. 1992;54:1046–52*
Durzinsky DS. *see* Pellegrini, Mucci, & others. 1992;54:578–9,HW
Dzik WH, Fleisher AG, Ciavarella D, Karlson KJ, Reed GE, Berger RL. Safety and efficacy of autologous blood donation before elective aortic valve operation. 1992;54:1177–81*

Ebner I. *see* Müller, Salzer, & others. 1992;54:493–7*
Echevarria JR. *see* Bernal, Rabasa, & others. 1992;54:152–4,CR
Edmondson SJ. *see* John, Edmondson, & Rees. 1992;54:190,CP
Edmunds LH Jr. *see* Downing & Edmunds. 1992;54:1236–43,CV
Edwards FH. *see* Cohen, Banks, & others. 1992;54:1216–8,CR
Efstratiadis T, Munsch C, Crossman D, Taylor KM. High-dose aprotinin in emergency coronary artery bypass after thrombolysis. Reply. 1992;54:1022–3,CP
Egan TM. *see* Karwande, Renlund, & others. 1992;54:1039–45,DI
Egan TM. *see* Lanza, Natarajan, & others. 1992;54:244–8,DI
Egan TM. *see* Shennib, Noirclerc, & others. 1992;54:27–32,DI
Eguchi S. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW
Eguchi S. *see* Tatebe, Nakazawa, & others. 1992;54:124–9*
Eijsman L. *see* Jansen, van Oeveren, & others. 1992;54:744–8*
Ekroth R. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*
Elami A. *see* Laks, Gates, & others. 1992;54:169–72,HW
Eldredge WJ. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Elefteriades JA. *see* Letsou, Hogan, & others. 1992;54:925–31*
Elkins RC. *see* Kon, Link, & others. 1992;54:39–43,DI
Elkins RE. *see* Ungerleider, Greeley, & others. 1992;54:691–8,DI
Elliott MJ. *see* Pawade, de Leval, & others. 1992;54:967–70*
Ellis FH Jr. The Nissen fundoplication. 1992;54:1231–6,CL
Ellis FH Jr. *see* Pera, Trastek, & others. 1992;54:199–204,DI
Ellis FH Jr. *see* Streitz, Williamson, & Ellis. 1992;54:586–91,CV
End A. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR
Endo M. *see* Tsuchida, Hashimoto, & others. 1992;54:161–3,CR
Engelman RM. *see* Christakis, Koch, & others. 1992;54:449–59,DI
Ensley RD. *see* Karwande, Ensley, & others. 1992;54:840–5*
Ercan H. *see* Schönberger, Everts, & others. 1992;54:1172–6*
Ergina PL, Tchervenkov CI. Balloon angioplasty in the treatment of aortic coarctation. 1992;54:599–600,CP
Ernst P. *see* Shennib, Noirclerc, & others. 1992;54:27–32*
Ernst SMPG. *see* van Heurn, Hamerlijnck, & others. 1992;54:157–8,CR
Esposito RA. *see* Bräu, Esposito, & Simberkoff. 1992;54:552–4,CR
Estanove S. *see* Girard, Quentin, & others. 1992;54:259–63*

Evans KG. *see* Hemming, Finley, & others. 1992;54:166–8,HW
Everts PAM. *see* Schönberger, Everts, & others. 1992;54:1172–6*
Evora PRB. *see* Pearson, Evora, & Schaff. 1992;54:1078–84*

Faber LP, Vester SR, Kittle CF, Warren WH, Jensik RJ. Manual versus stapled bronchial closure: still controversial. Reply. 1992;54:1021–2,CP
Fabiani J-N. *see* Acar, Jebara, & others. 1992;54:652–60*
Fabiani J-N. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Fabiani J-N. *see* Uva, Jebara, & others. 1992;54:89–92*
Fadhli HA. Pulmonary pseudotumor. 1992;54:1246,CP
Failing TL. *see* Borkon, Failing, & others. 1992;54:884–91*
Fardin R. *see* Cunningham, Gharavi, & others. 1992;54:947–51*
Farge A. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Fasoli G. *see* Bortolotti, Calabrò, & others. 1992;54:1219–20,CR
Fasules JW. *see* Ziomek, Harrell, & others. 1992;54:861–8*
Faulkner SC. *see* Ziomek, Harrell, & others. 1992;54:861–8*
Favaloro R. *see* Ridley, Khaghani, & others. 1992;54:333–7*
Feindel CM, Sandhu R, Cruz J, Wilson GJ. Effect of delay in retroperfusion therapy on infarct size reduction. 1992;54:1120–5*
Feldman JM. *see* Harpole, Feldman, & others. 1992;54:50–5*
Feng WC. *see* Singh, Feng, & Sanofsky. 1992;54:538–40*
Ferguson TB Jr. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Ferguson TB Sr. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Ferguson TB. *see* Irwin, Bianco, & others. 1992;54:669–75,DI
Fernandes ED, Kadivar H, Hallman GL, Reul GJ, Ott DA, Cooley DA. Congenital malformations of the coronary arteries: the Texas Heart Institute experience. 1992;54:732–40*
Fernandes S. *see* Sisto, Hoffman, & others. 1992;54:507–11*
Fernandez J, Joyce DH, Hirschfeld K, Chen C, Laub GW, Adkins MS, Anderson WA, Mackenzie JW, McGrath LB. Factors affecting mitral valve reoperation in 317 survivors after mitral valve reconstruction. 1992;54:440–8*
Fernandez J. *see* David, Armstrong, & Sun. 1992;54:661–8,DI
Fernandez J. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Ferson PF. *see* Landreneau, Dowling, & others. 1992;54:142–4,CR
Ferson PF. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Ferson PF. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
Fiedler RC. *see* Canver & Fiedler. 1992;54:1244,CP
Fields BL. *see* Stringham, Paulsen, & others. 1992;54:852–60*
Finley J. *see* Razzouk, Gow, & others. 1992;54:974–7,CR
Finley RJ. *see* Hemming, Finley, & others. 1992;54:166–8,HW
Fiore AC, Naunheim KS, D'Orazio S, Kaiser GC, McBride LR, Pennington DG, Peigh PS, Willman VL, Labovitz AJ, Barner HB. Mitral valve replacement: randomized trial of St. Jude and Medtronic-Hall prostheses. 1992;54:68–73*
Fiore AC. *see* Borkon, Failing, & others. 1992;54:884–91,DI
Fisher JD. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR
Flameng W. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP
Flanagan TL. *see* Cummings, Wyatt, & others. 1992;54:276–8*
Flanagan TL. *see* Daniel, Fleischer, & others. 1992;54:686–90*
Flanagan TL. *see* Kron, Kern, & others. 1992;54:617–20*
Flege JB Jr. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*
Fleischer KJ. *see* Daniel, Fleischer, & others. 1992;54:686–90*
Fleisher AG. *see* Dzik, Fleisher, & others. 1992;54:1177–81*
Fleury J-P. *see* Menasché, Fleury, & Piwnica. 1992;54:392–3,UP
Folmer HA. *see* van Son, Skotnicki, & others. 1992;54:130–3*
Fonger JD. *see* Aldea, Connelly, & others. 1992;54:789–90,HW
Forstot R. *see* Hogue, Barzilai, & others. 1992;54:562–3,CR
Fosse E. *see* Videm, Fosse, & others. 1992;54:725–31*
Fountain SW. *see* Gaer, Tsang, & others. 1992;54:512–6*
Fountain SW. *see* Liakakos, Ohri, & others. 1992;54:814,CP
Fountain SW. *see* Patel, Townsend, & Fountain. 1992;54:84–8*
Fradet G. *see* Hemming, Finley, & others. 1992;54:166–8,HW
Frame R. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR
Franco KL. *see* Hammond, Franco, & Baldwin. 1992;54:379–80,HW
Frantz PT. *see* Christakis, Koch, & others. 1992;54:449–59,DI
Frantz PT. *see* Menasché, Peynet, & others. 1992;54:472–8,DI
Fraser CD, Heitmiller RF. Cervical esophago-esophageal anastomosis. 1992;54:384–6,HW
Frater RWM. *see* Hoffman & Frater. 1992;54:399,CP
Frater RWM. *see* Hoffman & Frater. 1992;54:1228,HW
Frater RWM. *see* Sisto, Hoffman, & others. 1992;54:507–11*
Frazier E. *see* Ziomek, Harrell, & others. 1992;54:861–8*
Frazier OH. Thermo Cardiosystems left ventricular assist device. 1992;54:1019,CP
Frazier OH. *see* Baldwin, Klima, & others. 1992;54:978–9,CR
Frazier OH. *see* Golding, Crouch, & others. 1992;54:1059–64,DI
Frazier OH. *see* Sweeney & Frazier. 1992;54:1065–70*
Freihorst J. *see* Ziemer, Heinemann, & others. 1992;54:971–3,CR
Fremes SE. *see* Christakis, Koch, & others. 1992;54:449–59*
Frommhold H. *see* Müller, Salzer, & others. 1992;54:493–7*
Fry WA. *see* Winchester, Victor, & Fry. 1992;54:145–6,CR
Fudemoto Y. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW
Fukui K. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Fulton M. *see* Burt, Fulton, & others. 1992;54:226–32*
Fung A. *see* Kallis, Sneddon, & others. 1992;54:1182–5*
Fung J. *see* Armitage, Kormos, & others. 1992;54:205–11*
Furnary AP, Magovern JA, Christlieb IY, Orie JE, Simpson KA, Magovern GJ. Clinical cardiomyoplasty: preoperative factors associated with outcome. 1992;54:1139–43*
Furnary AP, Magovern JA, Simpson KA, Magovern GJ. Prolonged open sternotomy and delayed sternal closure after cardiac operations. 1992;54:233–9*
Fuse K. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Fuzellier JF. *see* Uva, Jebara, & others. 1992;54:89–92*

Gabbay S. Ionescu-Shiley valve failure II: experience with 25 low-profile explants. 1992;54:122–3,IC
Gabbay S. The Meadox-Gabbay pericardial xenograft: failure of the unicusp principle. 1992;54:957–8,IC
Gaer JAR, Tsang V, Khaghani A, Gillbe CE, Townsend ER, Fountain SW, Yacoub MH. Use of endotracheal silicone stents for relief of tracheobronchial obstruction. 1992;54:512–6*
Gallagher KP. *see* Bolling, Groh, & others. 1992;54:93–8*
Gallagher MW. *see* Christakis, Koch, & others. 1992;54:449–59,DI
Gallagher MW. *see* Hill, Bruhn, & others. 1992;54:699–704*
Galloway AC. *see* Crawford, Galloway, & others. 1992;54:212–5*
Gandsas A. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*
Garcia JM. *see* Pfister, Zaki, & others. 1992;54:1085–92*
Garofalo R. *see* Borioni, Ciani, & others. 1992;54:397–8,CP
Garred P. *see* Videm, Fosse, & others. 1992;54:725–31*
Gates RN. *see* Laks, Gates, & others. 1992;54:169–72,HW
Gay WA Jr. *see* Karwande, Ensley, & others. 1992;54:840–5*
Gay WA Jr. *see* Karwande, Renlund, & others. 1992;54:1039–45*
George JF, Kirklin JK. Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass. 1992;54:747–8,IC
Gerlis LM. *see* Ho, Gerlis, & others. 1992;54:264–70*
Ghali MG. *see* Phillips, Zeff, & others. 1992;54:908–10*
Gharavi MA. *see* Cunningham, Gharavi, & others. 1992;54:947–51*
Giaid A. *see* Adoumie, Serrick, & others. 1992;54:1071–7*

Gielchinsky I. *see* Sirivella, Gielchinsky, & Parsonnet. 1992;54:190,CP

Gillbe CE. *see* Gaer, Tsang, & others. 1992;54:512–6*

Gillette PC. *see* Kratz, Gillette, & others. 1992;54:485–9*

Ginsberg RJ. *see* Burt, Fulton, & others. 1992;54:226–32*

Ginsberg RJ. *see* Jones & Ginsberg. 1992;54:809,CP

Ginsberg RJ. *see* Martini, Burt, & others. 1992;54:460–6*

Ginsberg RJ. *see* Van Raemdonck, Schneider, & Ginsberg. 1992;54:999–1013,CV

Girard C, Quentin P, Bouvier H, Blanc P, Bastien O, Lehot J-J, Mikaeloff P, Estanove S. Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study. 1992;54:259–63*

Giudicelli R. *see* Shennib, Noirclerc, & others. 1992;54:27–32*

Glick Y. *see* Deviri, Izhar, & others. 1992;54:1018–9,CP

Glower DD, Bashore TM, Spritzer CE. Congenital aortic stenosis and patent ductus arteriosus in the adult. 1992;54:368–70,CR

Göhring U. *see* Machens, Mechtersheimer, & others. 1992;54:774–6,CR

Golding LAR, Crouch RD, Stewart RW, Novoa R, Lytle BW, McCarthy PM, Taylor PC, Loop FD, Cosgrove DM III. Postcardiotomy centrifugal mechanical ventricular support. 1992;54:1059–64*

Golding LAR. *see* Cosgrove, Heric, & others. 1992;54:1031–8*

Goldman BS. *see* Christakis, Koch, & others. 1992;54:449–59*

Goldstein J. *see* Smith & Goldstein. 1992;54:766–8,CR

Goldstraw P. *see* Shah, Thompson, & Goldstraw. 1992;54:498–501*

Goldstraw P. *see* Wong & Goldstraw. 1992;54:286–8*

Golino A, Stassano P, Spampinato N. Hemolysis after open heart operations. 1992;54:1246–7,CP

Gordon DF. *see* Phillips, Zeff, & others. 1992;54:908–10*

Gorenstein LA, Abel JG, Patterson GA. Pericardial repair of a tracheal laceration during transhiatal esophagectomy. 1992;54:784–6,CR

Gow R. *see* Razzouk, Gow, & others. 1992;54:974–7,CR

Goya T. *see* Asamura, Goya, & others. 1992;54:147–9,CR

Graffigna A, Pagani F, Minzioni G, Salerno J, Viganò M. Left atrial isolation associated with mitral valve operations. 1992;54:1093–8*

Graffigna A, Vigano M, Pagani F, Salerno G. Surgical treatment for ectopic atrial tachycardia. 1992;54:338–43*

Graham BS. *see* Lagerstrom, Mitchell, & others. 1992;54:764–5,CR

Graham TR. *see* Dunning, Kendall, & others. 1992;54:571–2,CR

Grare P. *see* Acar, Jebara, & others. 1992;54:652–60*

Gray GC. *see* Mickleborough, Mizuno, & others. 1992;54:832–9*

Greeley WJ. *see* Ungerleider, Greeley, & others. 1992;54:691–8*

Green R. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*

Grehan J. *see* Irwin, Bianco, & others. 1992;54:669–75*

Griepp RB. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*

Griffin SC, Dark JH. Abrupt cardiac failure using a right VAD in the presence of a tricuspid valve prosthesis. 1992;54:1023–4,CP

Griffith BP, Hardesty RL, Armitage JM, Kormos RL, Marrone GC, Duncan S, Paradis I, Dauber JH, Yousem SA, Williams P. Acute rejection of lung allografts with various immunosuppressive protocols. 1992;54:846–51*

Griffith BP. *see* Armitage, Kormos, & others. 1992;54:205–11*

Griffith BP. *see* Hirt, Haverich, & others. 1992;54:676–80,DI

Griffith BP. *see* Spray, Mallory, & others. 1992;54:216–25,DI

Griffiths M. *see* Kallis, Treasure, & others. 1992;54:741–3*

Grignon A. *see* Phillips, Zeff, & others. 1992;54:908–10*

Grillo HC, Suen HC, Mathisen DJ, Wain JC. Resectional management of thyroid carcinoma invading the airway. 1992;54:3–10*

Grillo HC. *see* Mathisen & Grillo. 1992;54:1053–8*

Grimm M. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR

Grinage RA. *see* Bolling, Groh, & others. 1992;54:93–8*

Groh MA. *see* Bolling, Groh, & others. 1992;54:93–8*

Gross J. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR

Grover FL. Preoperative morphologic and physiologic assessment of internal thoracic arteries. Reply. 1992;54:1021,CP

Gu YJ. *see* Jansen, van Oeveren, & others. 1992;54:744–8*

Guermonprez JL. *see* Acar, Jebara, & others. 1992;54:652–60*

Guiraudon GM. Extended approach to the mitral valve. Reply. 1992;54:597–8,CP

Gundry SR. *see* Menasché, Peynet, & others. 1992;54:472–8,DI

Gundry SR. *see* Pfister, Zaki, & others. 1992;54:1085–92,DI

Gundry SR. *see* Rizzo, Whittemore, & others. 1992;54:1099–109,DI

Gundry SR. *see* Spence, Lust, & others. 1992;54:21–6,DI

Gunning AJ. Ross' first homograft replacement of the aortic valve. 1992;54:809,CP

Gupta NK. *see* Martin, Horkay, & others. 1992;54:812–3,CP

Gurny P. *see* Pfister, Zaki, & others. 1992;54:1085–92*

Guslits BG. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR

Guyton RA. *see* Pearson, Evora, & Schaff. 1992;54:1078–84,DI

Haas G. *see* Pogrebniak, Haas, & others. 1992;54:33–8*

Hafner GH. *see* Trachiotis, Hafner, & others. 1992;54:898–902*

Haga Y, Yoshizu H, Okuda E, Uriuda Y, Mitsumaru A, Tamai S, Tanaka S. Surgical reconstruction of an ascending aortic dissection in Takayasu's arteritis. 1992;54:359–60,CR

Haines DE. *see* Kron, Kern, & others. 1992;54:617–20*

Hallman GL. *see* Fernandes, Kadivar, & others. 1992;54:732–40*

Hamerlijnck RPHM. *see* van Heurn, Hamerlijnck, & others. 1992;54:157–8,CR

Hammon JW Jr. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75,DI

Hammon JW Jr. *see* Kron, Kern, & others. 1992;54:617–20,DI

Hammon JW Jr. *see* Lagerstrom, Mitchell, & others. 1992;54:764–5,CR

Hammon JW Jr. *see* Lupinetti, Pridjian, & others. 1992;54:467–71,DI

Hammon JW Jr. *see* Vouhé, Tamisier, & others. 1992;54:621–7,DI

Hammond GL, Franco KL, Baldwin JC. Method of single-lung transplantation in the absence of a left atrial cuff. 1992;54:379–80,HW

Hammond ME. *see* Karwande, Ensley, & others. 1992;54:840–5*

Hammond RL. *see* Hooper, Niinami, & others. 1992;54:316–22*

Haneda K. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW

Haniuda M, Morimoto M, Nishimura H, Kobayashi O, Yamanda T, Iida F. Adjuvant radiotherapy after complete resection of thymoma. 1992;54:311–5*

Hanley FL. *see* Kern, Jonas, & others. 1992;54:749–54*

Hardesty RL. *see* Armitage, Kormos, & others. 1992;54:205–11*

Hardesty RL. *see* Griffith, Hardesty, & others. 1992;54:846–51*

Harpole DH Jr, Feldman JM, Buchanan S, Young WG, Wolfe WG. Bronchial carcinoid tumors: a retrospective analysis of 126 patients. 1992;54:50–5*

Harrell JE Jr. *see* Ziomek, Harrell, & others. 1992;54:861–8*

Hashimoto A. *see* Tsuchida, Hashimoto, & others. 1992;54:161–3,CR

Hata A. *see* Tamiya, Yamashiro, & others. 1992;54:717–24*

Haverich A. *see* Adoumie, Serrick, & others. 1992;54:1071–7,DI

Haverich A. *see* Hirt, Haverich, & others. 1992;54:676–80*

Haverich A. *see* Irwin, Bianco, & others. 1992;54:669–75,DI
Hawkins JA. *see* Karwande, Renlund, & others. 1992;54:1039–45*
Hawley PC. *see* McCaughan, Hawley, & others. 1992;54:705–11*
Hayashi J-I. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW
Hayashi J-I. *see* Tatebe, Nakazawa, & others. 1992;54:124–9*
Haydar S. *see* Menasché, Peynet, & others. 1992;54:472–8*
Haydock DA, Low DE, Trulock EP, Kaiser LR, Pasque MK, Molmenti E, Cooper JD. Pulmonary "twinning" procedure: use of lungs from one donor for single-lung transplantation in two recipients. 1992;54:1189–92*
Hazelrigg SR, Auer JE, Seifert PE. Experience in 100 transthoracic balloon pumps. 1992;54:528–32*
Hazelrigg SR. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Hazelrigg SR. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
Heath BJ. *see* Warren, Heath, & Brand. 1992;54:240–3*
Hedderich G. *see* Morin, Hedderich, & others. 1992;54:911–4*
Heerdt PM, Pond CG, Blessios GA, Rosenbloom M. Comparison of cardiac output measured by intrapulmonary artery Doppler, thermodilution, and electromagnetometry. 1992;54:959–66*
Heimbecker RO. *see* Laub, Muralidharan, & others. 1992;54:826–31,DI
Heinemann M. *see* Ziemer, Heinemann, & others. 1992;54:971–3,CR
Heitmiller RF. *see* Fraser & Heitmiller. 1992;54:384–6,HW
Hemming AW, Finley RJ, Evans KG, Nelems B, Fradet G. Esophagogastrectomy and the variant left hepatic artery. 1992;54:166–8,HW
Hendren WH. *see* Shamberger, Wohl, & others. 1992;54:1206–8,CR
Heric B. *see* Cosgrove, Heric, & others. 1992;54:1031–8*
Herlan DB. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Herman SD. *see* Watanabe, Fuse, & others. 1992;54:479–84,DI
Hess KR. *see* Svensson, Crawford, & others. 1992;54:427–39*
Hickey PR. *see* Kern, Jonas, & others. 1992;54:749–54*
Hickey PR. *see* Kern, Morana, & others. 1992;54:541–6*
Hicks GL Jr. *see* Pearson, Evora, & Schaff. 1992;54:1078–84,DI
Hiebert CA. *see* Topart, Deschamps, & others. 1992;54:1046–52,DI
Higashiyama M. *see* Kodama, Doi, & others. 1992;54:1193–5*
Hikosaka H. *see* Watanabe, Abe, & others. 1992;54:993–4,HW
Hilgenberg AD. *see* Muehrcke, Daggett, & others. 1992;54:876–83*
Hill JG, Bruhn PS, Cohen SE, Gallagher MW, Manart F, Moore CA, Seifert PE, Askari P, Banchieri C. Emergent applications of cardiopulmonary support: a multiinstitutional experience. 1992;54:699–704*
Hiraishi T. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW
Hirano A. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Hirschfeld K. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Hirt SW, Haverich A, Wahlers T, Schäfers H-J, Alken A, Borst H-G. Predictive criteria for the need of extracorporeal circulation in single-lung transplantation. 1992;54:676–80*
Hisatomi K, Isomura T, Hirano A, Sato T, Nishimi M, Kawara T, Ohishi K. Long-term follow-up results after reconstruction of the mitral valve by leaflet advancement. 1992;54:271–5*
Hix WR. *see* Crawford, Galloway, & others. 1992;54:212–5,DI
Hix WR. *see* Trachiotis, Hafner, & others. 1992;54:898–902*
Ho SY, Gerlis LM, Toms J, Lincoln C, Anderson RH. Morphology of the posterior junctional area in atrioventricular septal defects. 1992;54:264–70*
Hoffman D, Frater RWM. Bronchial stump closure. 1992;54:399,CP
Hoffman DM, Frater RWM. Inverted Y incision for accurate tailoring of patches and vessels. 1992;54:1228,HW
Hoffman DM. *see* Sisto, Hoffman, & others. 1992;54:507–11*
Hogan JF. *see* Letsou, Hogan, & others. 1992;54:925–31*
Hogue CW Jr, Barzilai B, Forstot R, Shuman TS, Cox JL. Intraoperative echocardiographic diagnosis of previously unrecognized cor triatriatum. 1992;54:562–3,CR
Holland FW II, Brown PS Jr, Clark RE. Acute severe postischemic myocardial depression reversed by triiodothyronine. 1992;54:301–5*
Holman WL. Electrical instability during reperfusion. 1992;54:1245–6,CP
Holmes SJK. *see* Kallis, Treasure, & others. 1992;54:741–3*
Holzman IR. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*
Honma T. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Hooper TL, Niinami H, Hammond RL, Lu H, Ruggiero R, Pochettino A, Stephenson LW. Skeletal muscle ventricles as left atrial–aortic pumps: short-term studies. 1992;54:316–22*
Hoover EL. *see* Daniel, Fleischer, & others. 1992;54:686–90,DI
Hopkins RA. Ross' first homograft replacement of the aortic valve. Reply. 1992;54:809–10,CP
Horii T. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Horkay F. *see* Martin, Horkay, & others. 1992;54:812–3,CP
Horowitz MD, Portogues CG, Matos LA, McGowan RW III. Hyperbaric oxygen: value in management of nonhealing saphenectomy wounds. 1992;54:782–3,CR
Hoskins ML. *see* Borkon, Failing, & others. 1992;54:884–91*
Hosokawa H. *see* Watanabe, Abe, & others. 1992;54:993–4,HW
Hsieh C-M, Mishkel GJ, Cardoso PFG, Rakowski H, Dunn SC, Butany J, Weisel RD, Patterson GA, Cooper JD. Production and reversibility of right ventricular hypertrophy and right heart failure in dogs. 1992;54:104–10*
Hubbell DS. *see* McKeown, Conant, & Hubbell. 1992;54:490–2*
Huber H. *see* Müller, Salzer, & others. 1992;54:493–7*
Huddleston CB. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Huddleston CB. *see* Spray, Mallory, & others. 1992;54:216–25*
Hung C-R. *see* Leu, Chiu, & others. 1992;54:134–6*
Hunter J. *see* Knott-Craig, van der Merwe, & others. 1992;54:557–9,CR
Hunter S, Angelini GD. Hemodynamic effects of pericardial closure. Reply. 1992;54:1023,CP
Hutchinson JE III. *see* David, Armstrong, & Sun. 1992;54:661–8,DI
Huvos AG. *see* Burt, Fulton, & others. 1992;54:226–32*

Iannone LA. *see* Phillips, Zeff, & others. 1992;54:908–10*
Icard P, Regnard J-F, de Napoli S, Rojas-Miranda A, Dartevelle P, Levasseur P. Primary lung cancer in young patients: a study of 82 surgically treated patients. 1992;54:99–103*
Iida F. *see* Haniuda, Morimoto, & others. 1992;54:311–5*
Ilbawi MN. *see* Wilson, Ilbawi, & others. 1992;54:892–3*
Imai M. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR
Imai S. *see* Tatebe, Nakazawa, & others. 1992;54:124–9*
Irwin ED, Bianco RW, Clack R, Grehan J, Slovut DP, Nakhleh R, Bolman RM III, Shumway SJ. Use of epicardial electrocardiograms for detecting cardiac allograft rejection. 1992;54:669–75*
Isomura T. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Ius P. *see* Bortolotti, Ius, & others. 1992;54:952–8*
Ivankovich AD. *see* Tuman, McCarthy, & Ivankovich. 1992;54:811–2,CP
Ivatury RR, Rohman M. Penetrating cardiac trauma. 1992;54:1247–8,CP

Iverson LIG. *see* Reed & Iverson. 1992;54:985–6,CR
Iwabuchi S. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Izhar U. *see* Deviri, Izhar, & others. 1992;54:1018–9,CP
Izzat NN. *see* Jones, Izzat, & others. 1992;54:44–9*

Jacobey JA. *see* Creswell, Rosenbloom, & others. 1992;54:11–20,DI
Jacobowitz IJ. *see* Maughan, Mohan, & others. 1992;54:818–25*
Jacobs ML. *see* Jobes, Nicolson, & others. 1992;54:150–1,CR
Jacobs ML. *see* Norwood, Jacobs, & Murphy. 1992;54:1025–30*
Jamieson WRE. *see* David, Armstrong, & Sun. 1992;54:661–8,DI
Jamplis RW. Introduction. 1992;54:193*
Jansen NJG, van Oeveren W, Gu YJ, van Vliet MH, Eijsman L, Wildevuur CRH. Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass. 1992;54:744–8*
Jebara VA, Chauvaud S, Portoghese M, Uva MS, Acar C, Farge A, Dervanian P, Sarkis A, Bruneval P, Fabiani J-N, Deloche A, Carpentier AF. Isolated extracardiac unruptured sinus of Valsalva aneurysms. 1992;54:323–6*
Jebara VA. *see* Acar, Jebara, & others. 1992;54:652–60*
Jebara VA. *see* Uva, Jebara, & others. 1992;54:89–92*
Jensik RJ. *see* Faber, Vester, & others. 1992;54:1021–2,CP
Jeyasingham K. *see* Molnar & Jeyasingham. 1992;54:569–70,CR
Joachimsson P-O. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*
Jobes DR, Nicolson SC, Steven JM, Miller M, Jacobs ML, Norwood WI Jr. Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome. 1992;54:150–1,CR
John LCH, Edmondson SJ, Rees GM. Modified technique of internal mammary artery harvest. Reply. 1992;54:190,CP
Johnson JA. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Jolly SR. *see* Spence, Lust, & others. 1992;54:21–6*
Jonas RA. *see* Kern, Jonas, & others. 1992;54:749–54*
Jonas RA. *see* Mezrow, Sadeghi, & others. 1992;54:609–16,DI
Jones JW, Izzat NN, Rashad MN, Thornby JI, McLean TR, Svensson LG, Beall AC Jr. Usefulness of right ventricular indices in early diagnosis of cardiac tamponade. 1992;54:44–9*
Jones JW. *see* Svensson, Crawford, & others. 1992;54:74–9*
Jones WG II, Ginsberg RJ. Esophageal perforation. Reply. 1992;54:809,CP
Joyce DH. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Justicz AG. *see* Symbas, Justicz, & Ricketts. 1992;54:177–83,CT
Juvonen J. *see* Juvonen, Lepojärvi, & others. 1992;54:560–1,CR
Juvonen T, Lepojärvi M, Pokela R, Juvonen J, Kairaluoma MI. Mediastinal window: a cause of simultaneous bilateral spontaneous pneumothorax. 1992;54:560–1,CR

Kadivar H. *see* Fernandes, Kadivar, & others. 1992;54:732–40*
Kairaluoma MI. *see* Juvonen, Lepojärvi, & others. 1992;54:560–1,CR
Kaiser GC. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Kaiser LR. *see* Burt, Fulton, & others. 1992;54:226–32,DI
Kaiser LR. *see* Haydock, Low, & others. 1992;54:1189–92*
Kaiser LR. *see* Spray, Mallory, & others. 1992;54:216–25*
Kako N. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Kakos GS. *see* McCaughan, Hawley, & others. 1992;54:705–11*
Kalis NN. *see* Knott-Craig, van der Merwe, & others. 1992;54:557–9,CR
Kallis P, Sneddon JF, Simpson IA, Fung A, Pepper JR, Smith EEJ. Clinical and hemodynamic evaluation of the 19-mm Carpentier-Edwards supraannular aortic valve. 1992;54:1182–5*
Kallis P, Treasure T, Holmes SJK, Griffiths M. Exocrine pancreatic function in mediastinal teratomata: an aid to preoperative diagnosis? 1992;54:741–3*
Kaneko M. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW
Kanter RJ. *see* Ungerleider, Greeley, & others. 1992;54:691–8*
Kao RL. *see* Demmy, Magovern, & Kao. 1992;54:915–20*
Kaplan LJ, Weiman DS, Langan N, Sokil AB, Whitman GJR. Safe intraaortic balloon pump placement through the ascending aorta using transesophageal ultrasound. 1992;54:374–5,HW
Karck M, Vivi A, Tassini M, Schwalb H, Askenasy N, Merchav H, Navon G, Uretzky G. Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance. 1992;54:348–51*
Karl TR, Sano S, Pornviliwan S, Mee RBB. Tetralogy of Fallot: favorable outcome of nonneonatal transatrial, transpulmonary repair. 1992;54:903–7*
Karl TR. *see* Watterson, Malm, & others. 1992;54:1116–9*
Karlson KJ. *see* Dzik, Fleisher, & others. 1992;54:1177–81*
Karpeh M. *see* Burt, Fulton, & others. 1992;54:226–32*
Karwande SV, Ensley RD, Renlund DG, Gay WA Jr, Richenbacher WE, Doty DB, Hammond ME, Marks JD, Registry of the International Society for Heart Lung Transplantation. Cardiac retransplantation: a viable option? 1992;54:840–5*
Karwande SV, Renlund DG, Olsen SL, Gay WA Jr, Richenbacher WE, Hawkins JA, Millar RC, Marks JD. Mediastinitis in heart transplantation. 1992;54:1039–45*
Karwande SV, Rowles JR. Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates. 1992;54:164–5,HW
Karwande SV, Rowles JR. Bilateral anterior thoracotomy for automatic implantable cardioverter defibrillator placement in patients with previous sternotomy. 1992;54:791–3,HW
Kaulitz R. *see* Ziemer, Heinemann, & others. 1992;54:971–3,CR
Kawara T. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Kawashima Y. *see* Matsuki, Yagihara, & others. 1992;54:991–2,HW
Kay GL. *see* Muehrcke, Daggett, & others. 1992;54:876–83,DI
Kayali MT. *see* Raffa, Al-Ibrahim, & others. 1992;54:159–60,CR
Keeley SB. Homograft root replacement for juvenile rheumatoid aortic valve incompetence. Reply. 1992;54:602–3,CP
Kendall SWH, Ciulli F, Mullins PA, Biocina B, Dunning JJ, Large SR. Total orthotopic heart transplantation: an alternative to the standard technique. 1992;54:187,CP
Kendall SWH. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Kenney BD. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Keon CA. *see* Walley, Keon, & others. 1992;54:111–6*
Keon CA. *see* Walley, Keon, & others. 1992;54:117–23*
Keon WJ. *see* Walley, Keon, & others. 1992;54:111–6*
Keon WJ. *see* Walley, Keon, & others. 1992;54:117–23*
Kern FH, Jonas RA, Mayer JE Jr, Hanley FL, Castaneda AR, Hickey PR. Temperature monitoring during CPB in infants: does it predict efficient brain cooling? 1992;54:749–54*
Kern FH, Morana NJ, Sears JJ, Hickey PR. Coagulation defects in neonates during cardiopulmonary bypass. 1992;54:541–6*
Kern JA. *see* Kron, Kern, & others. 1992;54:617–20*
Khaghani A. *see* Gaer, Tsang, & others. 1992;54:512–6*
Khaghani A. *see* Ridley, Khaghani, & others. 1992;54:333–7*
Khalili M. *see* Walley, Keon, & others. 1992;54:111–6*
Khalili M. *see* Walley, Keon, & others. 1992;54:117–23*

Killen DA. *see* Borkon, Failing, & others. 1992;54:884–91*
Kim JH. *see* Letsou, Hogan, & others. 1992;54:925–31*
Kim SG. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR
Kirklin JK. *see* George & Kirklin. 1992;54:747–8,IC
Kisslo JA. *see* Ungerleider, Greeley, & others. 1992;54:691–8*
Kitano M. *see* Okita, Miki, & others. 1992;54:771–3,CR
Kittle CF. *see* Faber, Vester, & others. 1992;54:1021–2,CP
Kittle CF. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Klepetko W. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR
Klima T. *see* Baldwin, Klima, & others. 1992;54:978–9,CR
Knott-Craig CJ. Penetrating cardiac trauma. Reply. 1992;54:1248,CP
Knott-Craig CJ, van der Merwe PL, Kalis NN, Hunter J. Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction. 1992;54:557–9,CR
Kobayashi M. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Kobayashi O. *see* Haniuda, Morimoto, & others. 1992;54:311–5*
Kobayashi T. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW
Kobayashi T. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Koch JP. *see* Christakis, Koch, & others. 1992;54:449–59*
Kodama K, Doi O, Yasuda T, Higashiyama M, Yokouchi H. Radical laser segmentectomy for T1 N0 lung cancer. 1992;54:1193–5*
Koie H. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Kon ND, Link KM, Buchanan WP, Nomeir A-M, Downes TR, Cordell AR. Magnetic resonance imaging evaluation of recipient for cryopreserved aortic allograft. 1992;54:39–43*
Kondo H. *see* Asamura, Goya, & others. 1992;54:147–9,CR
Kongtahworn C. *see* Phillips, Zeff, & others. 1992;54:908–10*
Konishi H. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Kopelman HE. *see* Sealy, Kopelman, & Murphy. 1992;54:306–10*
Kormos RL. *see* Armitage, Kormos, & others. 1992;54:205–11*
Kormos RL. *see* Griffith, Hardesty, & others. 1992;54:846–51*
Kormos RL. *see* Sweeney & Frazier. 1992;54:1065–70,DI
Koterazawa T. *see* Yamashita, Nakamura, & others. 1992;54:761–3,CR
Kouchoukos NT. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Kouchoukos NT. *see* Svensson, Crawford, & others. 1992;54:427–39,DI
Koyama K. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Koyanagi H. *see* Tsuchida, Hashimoto, & others. 1992;54:161–3,CR
Kramer MD. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR
Krasna MJ. *see* Albuquerque, Krasna, & McLaughlin. 1992;54:980–2,CR
Kratz JM, Gillette PC, Crawford FA, Sade RM, Zeigler VL. Atrioventricular pacing in congenital heart disease. 1992;54:485–9*
Kratz JM. *see* Douville, Kratz, & others. 1992;54:56–61*
Kron IL, Kern JA, Theodore P, Flanagan TL, Haines DE, Barber MJ, DiMarco JP. Does a posterior aneurysm increase the risk of endocardial resection? 1992;54:617–20*
Kron IL. *see* Cummings, Wyatt, & others. 1992;54:276–8*
Kron IL. *see* Daniel, Fleischer, & others. 1992;54:686–90*
Kuge K. *see* Tamiya, Yamashiro, & others. 1992;54:717–24*
Kulatilake ENP. *see* Lamarra, Azzu, & Kulatilake. 1992;54:361–3,CR
Kumar M. *see* Tewari & Kumar. 1992;54:191,CP
Kumar N, Prabhakar G, Al-Fadley F, Al-Halees Z, Duran CMG. New surgical technique for type B aortic interruption. 1992;54:797–9,HW
Kumar N, Prabhakar G, Wilson N, Al Halees Z, Duran CMG. Total correction of transposition of great arteries with atrioventricular septal defect. 1992;54:989–90,CR
Kusuhara K. *see* Okita, Miki, & others. 1992;54:771–3,CR
Kyo E. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR

Laborde N. *see* Couraud, Baudet, & others. 1992;54:397,CP
Labovitz AJ. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Labrousse L. *see* Nashef, Dromer, & others. 1992;54:937–40*
Ladowski J. *see* Griffith, Hardesty, & others. 1992;54:846–51,DI
Lagerstrom CF, Mitchell HG, Graham BS, Hammon JW Jr. Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis. 1992;54:764–5,CR
Lai W-W. *see* Wu & Lai. 1992;54:155–6,CR
Lajam FE. *see* Miller, Allen, & others. 1992;54:410–4,DI
Laks H, Gates RN, Elami A, Pearl JM. Damus-Stansel-Kaye procedure: technical modifications. 1992;54:169–72,HW
Laks H. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75,DI
Laks H. *see* Norwood, Jacobs, & Murphy. 1992;54:1025–30,DI
Laks H. *see* Pearl, Laks, & others. 1992;54:1144–50*
Laks H. *see* Vouhé, Tamisier, & others. 1992;54:621–7,DI
Lamarra M, Azzu AA, Kulatilake ENP. Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin. 1992;54:361–3,CR
Landreneau RJ. Surgical stabilization of the flail chest. Reply. 1992;54:398,CP
Landreneau RJ, Dowling RD, Castillo WM, Ferson PF. Thoracoscopic resection of an anterior mediastinal tumor. 1992;54:142–4,CR
Landreneau RJ, Hazelrigg SR, Ferson PF, Johnson JA, Nawarawong W, Boley TM, Curtis JJ, Bowers CM, Herlan DB, Dowling RD. Thoracoscopic resection of 85 pulmonary lesions. 1992;54:415–20*
Landreneau RJ, Mack MJ, Hazelrigg SR, Dowling RD, Acuff TE, Magee MJ, Ferson PF. Video-assisted thoracic surgery: basic technical concepts and intercostal approach strategies. 1992;54:800–7,CV
Landreneau RJ. *see* Chechani, Landreneau, & Shaikh. 1992;54:296–300*
Langan N. *see* Kaplan, Weiman, & others. 1992;54:374–5,HW
Lanza LA, Natarajan G, Roth JA, Putnam JB Jr. Long-term survival after resection of pulmonary metastases from carcinoma of the breast. 1992;54:244–8*
Lanza LA. *see* Cybulsky, Lanza, & others. 1992;54:533–7*
Larbalestier RI, Chard RB, Cohn LH. Optimal approach to the mitral valve: dissection of the interatrial groove. 1992;54:1186–8*
Large SR. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Large SR. *see* Kendall, Ciulli, & others. 1992;54:187,CP
Laschinger JC, Ringel RE, Brenner JI, McLaughlin JS. Extracardiac total cavopulmonary connection. 1992;54:371–3,CR
Latreille R. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Laub GW, Muralidharan S, Clancy R, Eldredge WJ, Chen C, Adkins MS, Fernandez J, Anderson WA, McGrath LB. Cryopreserved allograft veins as alternative coronary artery bypass conduits: early phase results. 1992;54:826–31*
Laub GW. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Lavigne J-P. *see* Defraigne, Vahdat, & others. 1992;54:983–4,CR
Le Houerou D, Singh AI, Romano M, Martin V, Lessana A. Minimal hemodilution and optimal potassium use during normothermic aerobic arrest. 1992;54:815–6,CP
Lebel F. *see* Shennib, Noirclerc, & others. 1992;54:27–32*
LeBlanc JG. *see* Webber, Sett, & LeBlanc. 1992;54:344–7*
Leca F. *see* Vouhé, Tamisier, & others. 1992;54:621–7*
Lee J. *see* Leung, Lee, & others. 1992;54:523–7*

Lee P. *see* Letsou, Hogan, & others. 1992;54:925–31*
Lefrak EA. *see* Burton, Phillips, & others. 1992;54:1019–20,CP
Lehot J-J. *see* Girard, Quentin, & others. 1992;54:259–63*
Lepojärvi M. *see* Juvonen, Lepojärvi, & others. 1992;54:560–1,CR
Lerut T. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP
Lessana A. *see* Le Houerou, Singh, & others. 1992;54:815–6,CP
Lester JL. *see* Spence, Lust, & others. 1992;54:21–6,DI
Letsou GV, Hogan JF, Lee P, Kim JH, Ariyan S, Dewar ML, Baldwin JC, Elefteriades JA. Comparison of 180-degree and 360-degree skeletal muscle nerve cuff electrodes. 1992;54:925–31*
Leu M-R, Chiu I-S, Hung C-R, Wu M-H. Surgical implications of juxtaposed atrial appendages and the associated anomalies. 1992;54:134–6*
Leung MP, Lee J, Lo RNS, Mok CK. Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis. 1992;54:523–7*
Levasseur P. *see* Icard, Regnard, & others. 1992;54:99–103*
Levitsky S. *see* Menasché, Peynet, & others. 1992;54:472–8,DI
Levy D. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*
Lewis RJ, Caccavale RJ, Sisler GE, Mackenzie JW. One hundred consecutive patients undergoing video-assisted thoracic operations. 1992;54:421–6*
Lewis RJ, Sisler GE, Caccavale RJ. Imaged thoracic lobectomy: should it be done? 1992;54:80–3*
Liakakos TK, Ohri SK, Townsend ER, Fountain SW. Palliative intubation for dysphagia. Reply. 1992;54:814,CP
Lichtenstein SV. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Lichtenstein SV. *see* Christakis, Koch, & others. 1992;54:449–59*
Liddle HV. Thoracic Surgery Foundation for Research and Education. 1992;54:595,AN
Lieberman Y. *see* Bar-El, Lieberman, & Yellin. 1992;54:995–6,HW
Liebermann-Meffert DMI, Meier R, Siewert JR. Vascular anatomy of the gastric tube used for esophageal reconstruction. 1992;54:1110–5*
Limet R. *see* Defraigne, Vahdat, & others. 1992;54:983–4,CR
Lin C-Y, Wang J-S. Thromboelastogram and postoperative hemorrhage. Reply. 1992;54:813,CP
Lincoln C. *see* Ho, Gerlis, & others. 1992;54:264–70*
Linehan WM. *see* Pogrebniak, Haas, & others. 1992;54:33–8*
Link KM. *see* Kon, Link, & others. 1992;54:39–43*
Linka A. *see* Carrel, Linka, & Turina. 1992;54:352–4,CR
Liu J-F, Su Z-K, Ding W-X. Quantitation of particulate microemboli during cardiopulmonary bypass: experimental and clinical studies. 1992;54:1196–202*
Llobera M. *see* Aguilo & Llobera. 1992;54:1021,CP
Lo RNS. *see* Leung, Lee, & others. 1992;54:523–7*
LoCicero J. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Logan RW. *see* Mitchell, Saunders, & others. 1992;54:814,CP
Lohmann DP, McBride LR, Pennington DG, Swartz MT. Replacement of paracorporeal ventricular assist devices. 1992;54:1226–7,HW
Lonquist J. *see* Baldwin, Klima, & others. 1992;54:978–9,CR
Loop FD. *see* Cosgrove, Heric, & others. 1992;54:1031–8*
Loop FD. *see* Golding, Crouch, & others. 1992;54:1059–64*
Louagie YAG. *see* Buche, Schroeder, & others. 1992;54:381–3,HW
Low DE. *see* Haydock, Low, & others. 1992;54:1189–92*
Lowe JE. *see* Mickleborough, Mizuno, & others. 1992;54:832–9,DI
Lowe JE. *see* Tedder, Anstadt, & others. 1992;54:387–91,CV
Loy M. *see* Bortolotti, Calabrò, & others. 1992;54:1219–20,CR
Lu H. *see* Hooper, Niinami, & others. 1992;54:316–22*
Lupinetti FM, Pridjian AK, Callow LB, Crowley DC, Beekman RH, Bove EL. Optimum treatment of discrete subaortic stenosis. 1992;54:467–71*
Lust RM. *see* Chitwood, Cosgrove, & others. 1992;54:517–22*
Lust RM. *see* Spence, Lust, & others. 1992;54:21–6*
Lytle BW. *see* Cosgrove, Heric, & others. 1992;54:1031–8*
Lytle BW. *see* Golding, Crouch, & others. 1992;54:1059–64*

Mabee TM. *see* Davies, Wells, & others. 1992;54:1020,CP
Machens H-G, Mechtersheimer R, Göhring U, Schlag PN. Bilateral elastofibroma dorsi. 1992;54:774–6,CR
Mack MJ, Aronoff RJ, Acuff TE, Douthit MB, Bowman RT, Ryan WH. Present role of thoracoscopy in the diagnosis and treatment of diseases of the chest. 1992;54:403–9*
Mack MJ. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20,DI
Mack MJ. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
MacKenzie JW. *see* Borkon, Failing, & others. 1992;54:884–91,DI
Mackenzie JW. *see* Fernandez, Joyce, & others. 1992;54:440–8*
Mackenzie JW. *see* Lewis, Caccavale, & others. 1992;54:421–6*
MacKenzie JW. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Macmanus Q. *see* Burton, Phillips, & others. 1992;54:1019–20,CP
Magee MJ. *see* Landreneau, Mack, & others. 1992;54:800–7,CV
Magovern GJ. *see* Demmy, Magovern, & Kao. 1992;54:915–20*
Magovern GJ. *see* Furnary, Magovern, & others. 1992;54:1139–43*
Magovern GJ. *see* Furnary, Magovern, & others. 1992;54:233–9*
Magovern JA. *see* Furnary, Magovern, & others. 1992;54:1139–43*
Magovern JA. *see* Furnary, Magovern, & others. 1992;54:233–9*
Majid NK. *see* Baeza, Majid, & others. 1992;54:62–7*
Mallory GB. *see* Spray, Mallory, & others. 1992;54:216–25*
Malm TK. *see* Watterson, Malm, & others. 1992;54:1116–9*
Manart F. *see* Hill, Bruhn, & others. 1992;54:699–704*
Mannick JA. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*
Mansoori S. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Mansour KA. *see* Daniel, Fleischer, & others. 1992;54:686–90,DI
Mansour KA. *see* Kratz, Gillette, & others. 1992;54:485–9,DI
Mansour KA. *see* Miller. 1992;54:249–52,DI
Mansour KA. *see* Pogrebniak, Haas, & others. 1992;54:33–8,DI
Marchese D. *see* Bortolotti, Calabrò, & others. 1992;54:1219–20,CR
Marcus M. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP
Marini CP. *see* Maughan, Mohan, & others. 1992;54:818–25*
Marks JD. *see* Karwande, Ensley, & others. 1992;54:840–5*
Marks JD. *see* Karwande, Renlund, & others. 1992;54:1039–45*
Marrone GC. *see* Armitage, Kormos, & others. 1992;54:205–11*
Marrone GC. *see* Griffith, Hardesty, & others. 1992;54:846–51*
Martigne C. *see* Couraud, Baudet, & others. 1992;54:397,CP
Martin PG, Horkay F, Gupta NK, Walker DR. Thromboelastogram and postoperative hemorrhage. 1992;54:812–3,CP
Martin SM. *see* Pearl, Laks, & others. 1992;54:1144–50*
Martin V. *see* Le Houerou, Singh, & others. 1992;54:815–6,CP
Martini N, Burt ME, Bains MS, McCormack PM, Rusch VW, Ginsberg RJ. Survival after resection of stage II non–small cell lung cancer. 1992;54:460–6*
Martini N. *see* Burt, Fulton, & others. 1992;54:226–32*
Massard G, Roeslin N, Wihlm J-M, Dumont P, Witz J-P, Morand G. Pleuropulmonary aspergilloma: clinical spectrum and results of surgical treatment. 1992;54:1159–64*
Mathisen DJ, Grillo HC. Clinical manifestation of mediastinal fibrosis and histoplasmosis. 1992;54:1053–8*
Mathisen DJ. *see* Grillo, Suen, & others. 1992;54:3–10*
Mathisen DJ. *see* Orringer. 1992;54:628–37,DI
Matos LA. *see* Horowitz, Portogues, & others. 1992;54:782–3,CR
Matsuda H. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW

Matsuki O, Yagihara T, Yamamoto F, Nishigaki K, Uemura H, Kawashima Y. New surgical technique for total-defect aortopulmonary window. 1992;54:991–2,HW

Mattson AM. *see* Bolling, Groh, & others. 1992;54:93–8*

Matuki K. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*

Maughan RE, Mohan C, Nathan IM, Ascer E, Damiani P, Jacobowitz IJ, Cunningham JN Jr, Marini CP. Intrathecal perfusion of an oxygenated perfluorocarbon prevents paraplegia after aortic occlusion. 1992;54:818–25*

Mauriat P. *see* Vouhé, Tamisier, & others. 1992;54:621–7*

Mavroudis C. *see* Citak, Rees, & Mavroudis. 1992;54:755–60*

Mavroudis C. *see* Ungerleider, Greeley, & others. 1992;54:691–8,DI

Mayer JE Jr. *see* Bolton & Mayer. 1992;54:769–70,CR

Mayer JE Jr. *see* Kern, Jonas, & others. 1992;54:749–54*

Mazzucco A. *see* Bortolotti, Ius, & others. 1992;54:952–8*

McBride LR. *see* Baeza, Majid, & others. 1992;54:62–7,DI

McBride LR. *see* Fiore, Naunheim, & others. 1992;54:68–73*

McBride LR. *see* Lohmann, McBride, & others. 1992;54:1226–7,HW

McCarthy PM. *see* Cosgrove, Heric, & others. 1992;54:1031–8*

McCarthy PM. *see* Golding, Crouch, & others. 1992;54:1059–64*

McCarthy RJ. *see* Tuman, McCarthy, & Ivankovich. 1992;54:811–2,CP

McCaughan JS Jr, Hawley PC, Brown DG, Kakos GS, Williams TE Jr. Effect of light dose on the photodynamic destruction of endobronchial tumors. 1992;54:705–11*

McConnell BA. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75*

McCormack PM. *see* Burt, Fulton, & others. 1992;54:226–32*

McCormack PM. *see* Martini, Burt, & others. 1992;54:460–6*

McGowan RW III. *see* Horowitz, Portogues, & others. 1992;54:782–3,CR

McGrath LB. *see* Fernandez, Joyce, & others. 1992;54:440–8*

McGrath LB. *see* Laub, Muralidharan, & others. 1992;54:826–31*

McKay R. Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction. 1992;54:559,IC

McKeown PP, Conant P, Hubbell DS. Thoracoscopic lung biopsy. 1992;54:490–2*

McKeown PP. *see* Hirt, Haverich, & others. 1992;54:676–80,DI

McKeown PP. *see* Karwande, Ensley, & others. 1992;54:840–5,DI

McKeown PP. *see* Miller, Allen, & others. 1992;54:410–4,DI

McKeown PP. *see* Ziomek, Harrell, & others. 1992;54:861–8,DI

McKneally MF. Lobectomy without a rib spreader. 1992;54:2,ED

McLaughlin JS. *see* Albuquerque, Krasna, & McLaughlin. 1992;54:980–2,CR

McLaughlin JS. *see* Attar & McLaughlin. 1992;54:192,CP

McLaughlin JS. *see* Laschinger, Ringel, & others. 1992;54:371–3,CR

McLean TR, Svensson LG, Stein B, Beall AC Jr, Thornby JI. Surgical considerations in bypassing coronary arteries with 100% proximal occlusion. 1992;54:894–7*

McLean TR. *see* Jones, Izzat, & others. 1992;54:44–9*

McLean TR. *see* Svensson, Crawford, & others. 1992;54:74–9*

McLoughlin D. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR

McMurtrey MM. *see* Cybulsky, Lanza, & others. 1992;54:533–7*

Mechtersheimer R. *see* Machens, Mechtersheimer, & others. 1992;54:774–6,CR

Mee RBB. *see* Karl, Sano, & others. 1992;54:903–7*

Mee RBB. *see* Watterson, Malm, & others. 1992;54:1116–9*

Meek RA. *see* Cunningham, Gharavi, & others. 1992;54:947–51*

Mehta PM. *see* Spence, Lust, & others. 1992;54:21–6*

Meier R. *see* Liebermann-Meffert, Meier, & Siewert. 1992;54:1110–5*

Melvin DB. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*

Menasché P, Fleury J-P, Piwnica A. Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery. 1992;54:392–3,UP

Menasché P, Peynet J, Touchot B, Aziz M, Haydar S, Perez G, Veyssié L, Montenegro J, Bloch G, Piwnica A. Normothermic cardioplegia: is aortic cross-clamping still synonymous with myocardial ischemia? 1992;54:472–8*

Meneshian A. *see* Pearl, Laks, & others. 1992;54:1144–50*

Mentzer SJ. *see* Sugarbaker, Mentzer, & Strauss. 1992;54:941–6*

Merchav H. *see* Karck, Vivi, & others. 1992;54:348–51*

Metras D. *see* Shennib, Noirclerc, & others. 1992;54:27–32*

Mezrow CK, Sadeghi AM, Gandsas A, Shiang HH, Levy D, Green R, Holzman IR, Griepp RB. Cerebral blood flow and metabolism in hypothermic circulatory arrest. 1992;54:609–16*

Mickleborough LL, Mizuno S-I, Downar E, Gray GC. Late results of operation for ventricular tachycardia. 1992;54:832–9*

Mikaeloff P. *see* Girard, Quentin, & others. 1992;54:259–63*

Miki S. *see* Okita & Miki. 1992;54:1247,CP

Miki S. *see* Okita, Miki, & others. 1992;54:771–3,CR

Milano A. *see* Bortolotti, Ius, & others. 1992;54:952–8*

Millar RC. *see* Karwande, Renlund, & others. 1992;54:1039–45*

Miller DC. *see* Casabona, De Paulis, & others. 1992;54:681–5,DI

Miller DC. *see* Graffigna, Pagani, & others. 1992;54:1093–8,DI

Miller DL, Allen MS, Trastek VF, Deschamps C, Pairolero PC. Videothoracoscopic wedge excision of the lung. 1992;54:410–4*

Miller GE Jr. Physician payment reform: a bibliography. 1992;54:184–5,KR

Miller JI Jr. Thallium imaging in preoperative evaluation of the pulmonary resection candidate. 1992;54:249–52*

Miller M. *see* Jobes, Nicolson, & others. 1992;54:150–1,CR

Mills NL. Skeletonization of the ITAs: a step backward? 1992;54:951,IC

Minarini M. *see* Bortolotti, Ius, & others. 1992;54:952–8*

Minzioni G. *see* Graffigna, Pagani, & others. 1992;54:1093–8*

Mishkel GJ. *see* Hsieh, Mishkel, & others. 1992;54:104–10*

Mispireta LA. *see* Pfister, Zaki, & others. 1992;54:1085–92*

Mitchell AG. *see* Ridley, Khaghani, & others. 1992;54:333–7*

Mitchell HG. *see* Lagerstrom, Mitchell, & others. 1992;54:764–5,CR

Mitchell IM, Saunders NR, Paton RD, Logan RW. The blue man phenomenon. 1992;54:814,CP

Mitchell ME, DeBoer DA, Crittenden MD, Clark RE. Nicardipine: myocardial protection in isolated working hearts. 1992;54:712–6*

Mitsumaru A. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR

Mitts DL. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*

Miyamura H. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW

Miyamura H. *see* Tatebe, Nakazawa, & others. 1992;54:124–9*

Miyoshi S. *see* Nakahara, Miyoshi, & Nakagawa. 1992;54:1016–7,UP

Mizuno S-I. *see* Mickleborough, Mizuno, & others. 1992;54:832–9*

Moerman PLE. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP

Mohan C. *see* Maughan, Mohan, & others. 1992;54:818–25*

Moher D. *see* Walley, Keon, & others. 1992;54:111–6*

Moher D. *see* Walley, Keon, & others. 1992;54:117–23*

Mohri H. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW

Mohri H. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*

Mok CK. *see* Leung, Lee, & others. 1992;54:523–7*

Mollnes TE. *see* Videm, Fosse, & others. 1992;54:725–31*

Molmenti E. *see* Haydock, Low, & others. 1992;54:1189–92*

Molnar TF, Jeyasingham K. Pericardioperitoneal shunt for persistent pericardial effusions: a new drainage procedure. 1992;54:569–70,CR
Montenegro J. *see* Menasché, Peynet, & others. 1992;54:472–8*
Moore CA. *see* Hill, Bruhn, & others. 1992;54:699–704*
Morana NJ. *see* Kern, Morana, & others. 1992;54:541–6*
Morand G. *see* Massard, Roeslin, & others. 1992;54:1159–64*
Morea M. *see* Casabona, De Paulis, & others. 1992;54:681–5*
Morimoto M. *see* Haniuda, Morimoto, & others. 1992;54:311–5*
Morin JE, Hedderich G, Poirier NL, Sampalis J, Symes JF. Coronary artery bypass using internal mammary artery branches. 1992;54:911–4*
Morita S. *see* Armitage, Kormos, & others. 1992;54:205–11*
Moront MG. *see* Ziomek, Harrell, & others. 1992;54:861–8,DI
Moss M. *see* Ziomek, Harrell, & others. 1992;54:861–8*
Mucci SJ. *see* Pellegrini, Mucci, & others. 1992;54:578–9,HW
Muehrcke DD, Daggett WM Jr, Buckley MJ, Akins CW, Hilgenberg AD, Austen WG. Postinfarct ventricular septal defect repair: effect of coronary artery bypass grafting. 1992;54:876–83*
Mulder DS. *see* Shennib, Noirclerc, & others. 1992;54:27–32*
Müller LC, Salzer GM, Huber H, Prior C, Ebner I, Frommhold H, Präuer H-W. Multimodal therapy of small cell lung cancer in TNM stages I through IIIa. 1992;54:493–7*
Mullins PA. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Mullins PA. *see* Kendall, Ciulli, & others. 1992;54:187,CP
Munsch C. *see* Efstratiadis, Munsch, & others. 1992;54:1022–3,CP
Muralidharan S. *see* Laub, Muralidharan, & others. 1992;54:826–31*
Murphy DA, Armour JA. Human cardiac nerve stimulation. 1992;54:502–6*
Murphy DA. *see* Sealy, Kopelman, & Murphy. 1992;54:306–10*
Murphy DJ Jr. *see* Rosenkranz, Murphy, & Cosgrove. 1992;54:779–81,CR
Murphy D. *see* Razzouk, Gow, & others. 1992;54:974–7,CR
Murphy JD. *see* Norwood, Jacobs, & Murphy. 1992;54:1025–30*
Musumeci F. *see* Ridley, Khaghani, & others. 1992;54:333–7*
Myers JL, McConnell BA, Waldhausen JA. Coarctation of the aorta in infants: does the aortic arch grow after repair? 1992;54:869–75*

Nakagawa K. *see* Nakahara, Miyoshi, & Nakagawa. 1992;54:1016–7,UP
Nakagawa S. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW
Nakahara K, Miyoshi S, Nakagawa K. A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer. 1992;54:1016–7,UP
Nakame T. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW
Nakamura H. *see* Yamashita, Nakamura, & others. 1992;54:566–8,CR
Nakamura H. *see* Yamashita, Nakamura, & others. 1992;54:761–3,CR
Nakamura H. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Nakamura K. *see* Yamashita, Nakamura, & others. 1992;54:566–8,CR
Nakamura K. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Nakano S. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW
Nakatsuka T. *see* Asamura, Goya, & others. 1992;54:147–9,CR
Nakazawa M. *see* Tatebe, Nakazawa, & others. 1992;54:124–9*
Nakazawa S. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW
Nakhleh R. *see* Irwin, Bianco, & others. 1992;54:669–75*
Naruke T. *see* Asamura, Goya, & others. 1992;54:147–9,CR
Naruse Y. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Nashef SAM, Dromer C, Velly J-F, Labrousse L, Couraud L. Expanding wire stents in benign tracheobronchial disease: indications and complications. 1992;54:937–40*
Natarajan G. *see* Lanza, Natarajan, & others. 1992;54:244–8*
Nathan IM. *see* Maughan, Mohan, & others. 1992;54:818–25*
Naunheim KS. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Navon G. *see* Karck, Vivi, & others. 1992;54:348–51*
Nawarawong W. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20*
Nelems B. *see* Hemming, Finley, & others. 1992;54:166–8,HW
Neptune WB. A new idea. 1992;54:188,CP
Newman D. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Nicolson SC. *see* Jobes, Nicolson, & others. 1992;54:150–1,CR
Nielsen JL. Cardiac and Noncardiac Complications of Open Heart Surgery: Prevention, Diagnosis and Treatment, edited by Morris N. Kotler, MD, and Anthony Alfieri, DO. 1992;54:1015,RV
Nielsen JL. Mediastinal Surgery, edited by Thomas W. Shields. 1992;54:781,RV
Niinami H. *see* Hooper, Niinami, & others. 1992;54:316–22*
Nishigaki K. *see* Matsuki, Yagihara, & others. 1992;54:991–2,HW
Nishikawa Y. *see* Yamashita, Nakamura, & others. 1992;54:566–8,CR
Nishimi M. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Nishimura H. *see* Haniuda, Morimoto, & others. 1992;54:311–5*
Noble WH. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Noirclerc M. *see* Shennib, Noirclerc, & others. 1992;54:27–32*
Nomeir A-M. *see* Kon, Link, & others. 1992;54:39–43*
Noon GP. *see* Sekela, Smart, & others. 1992;54:547–52*
Nordgren L. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*
Norwood WI Jr, Jacobs ML, Murphy JD. Fontan procedure for hypoplastic left heart syndrome. 1992;54:1025–30*
Norwood WI Jr. *see* Jobes, Nicolson, & others. 1992;54:150–1,CR
Nosher JL. *see* Ting, Nosher, & others. 1992;54:357–8,CR
Novick RJ. *see* Karwande, Renlund, & others. 1992;54:1039–45,DI
Novoa R. *see* Cosgrove, Heric, & others. 1992;54:1031–8*
Novoa R. *see* Golding, Crouch, & others. 1992;54:1059–64*
Nyström S-O. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*

Oberheu KH. *see* Laub, Muralidharan, & others. 1992;54:826–31,DI
Odell JA, Schurek JO, Barnard CN, Commerford PJ. Long-term results of the Ivalon baffle mitral valve repair. 1992;54:283–5*
Odim JNK. *see* Furnary, Magovern, & others. 1992;54:233–9,DI
Ohashi H. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR
Ohishi K. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Ohmi M, Tofukuji M, Sato K, Nakame T, Sato N, Haneda K, Mohri H. Permanent pacemaker implantation in premature infants less than 2,000 grams of body weight. 1992;54:1223–5,HW
Ohmi M. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*
Ohri SK. *see* Liakakos, Ohri, & others. 1992;54:814,CP
Oiseth S. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR
Okada M. *see* Yamashita, Nakamura, & others. 1992;54:566–8,CR
Okada M. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Okita Y, Miki S. Hemolysis after open heart operations. Reply. 1992;54:1247,CP
Okita Y, Miki S, Kusuhara K, Ueda Y, Tahata T, Sakai T, Tatsumi A, Kitano M. Aneurysm of coronary arteriovenous fistula

presenting as a calcified mediastinal mass. 1992;54:771–3,CR
Okuda E. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR
Olinger GN. Rereplacement of the mitral valve with representation of the subvalvular apparatus. 1992;54:188–90,CP
Olinger GN. *see* Kron, Kern, & others. 1992;54:617–20,DI
Olsen SL. *see* Karwande, Renlund, & others. 1992;54:1039–45*
Oobo H. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Orie JE. *see* Furnary, Magovern, & others. 1992;54:1139–43*
Orringer MB. Anterior mediastinal tracheostomy with and without cervical exenteration. 1992;54:628–37*
Oshima Y. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR
Otaki M. *see* Spence, Lust, & others. 1992;54:21–6*
Otero-Coto E. Retrograde disc escape in a Harken mitral valve prosthesis. Reply. 1992;54:394–5,CP
Ott DA. *see* Fernandes, Kadivar, & others. 1992;54:732–40*
Ott DA. *see* Sharma, Calderon, & Ott. 1992;54:137–41*
Oturanlar D, Klepetko W, Grimm M, End A, Wisser W, Wekerle T, Wolner E. Management of severe bronchial ischemia after bilateral sequential lung transplantation. 1992;54:1221–2,CR

Pagani F. *see* Graffigna, Pagani, & others. 1992;54:1093–8*
Pagani F. *see* Graffigna, Vigano, & others. 1992;54:338–43*
Pagny JY. *see* Acar, Jebara, & others. 1992;54:652–60*
Pairolero PC. Thoracoscopic resection of an anterior mediastinal tumor. 1992;54:144,IC
Pairolero PC. *see* Grillo, Suen, & others. 1992;54:3–10,DI
Pairolero PC. *see* Mack, Aronoff, & others. 1992;54:403–9,DI
Pairolero PC. *see* Miller, Allen, & others. 1992;54:410–4*
Pairolero PC. *see* Pera, Trastek, & others. 1992;54:199–204*
Panos AL, Ali IS, Birnbaum PL, Barrozo CAM, Al-Nowaiser O, Salerno TA. Coronary sinus injuries during retrograde continuous normothermic blood cardioplegia. 1992;54:1137–8*
Panos AL, Teoh KT, Wilson JK, Salerno TA. Replacement of the valvular prosthesis in a patient with a Bentall procedure. 1992;54:555–6,CR
Panos AL. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR
Paradis I. *see* Griffith, Hardesty, & others. 1992;54:846–51*
Parker EF. Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results. 1992;54:808,UP
Parry DH. *see* Sharpe, Sendegeya, & others. 1992;54:366–7,CR
Parsonnet V. *see* Sirivella, Gielchinsky, & Parsonnet. 1992;54:190,CP
Pasco EA. *see* Rizzo, Whittemore, & others. 1992;54:1099–109,DI
Pascoe EA. *see* Karwande, Renlund, & others. 1992;54:1039–45,DI
Pascoe EA. *see* Svensson, Crawford, & others. 1992;54:427–39,DI
Pasque MK. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*
Pasque MK. *see* Haydock, Low, & others. 1992;54:1189–92*
Pasque MK. *see* Shennib, Noirclerc, & others. 1992;54:27–32,DI
Pass HI. *see* Daniel, Fleischer, & others. 1992;54:686–90,DI
Pass HI. *see* Harpole, Feldman, & others. 1992;54:50–5,DI
Pass HI. *see* Lanza, Natarajan, & others. 1992;54:244–8,DI
Pass HI. *see* Pogrebniak, Haas, & others. 1992;54:33–8*
Patel RL, Townsend ER, Fountain SW. Elective pneumonectomy: factors associated with morbidity and operative mortality. 1992;54:84–8*
Patel V. *see* Svensson, Crawford, & others. 1992;54:74–9*
Paton RD. *see* Mitchell, Saunders, & others. 1992;54:814,CP
Patterson GA. *see* Gorenstein, Abel, & Patterson. 1992;54:784–6,CR
Patterson GA. *see* Hsieh, Mishkel, & others. 1992;54:104–10*
Paulsen KL. *see* Stringham, Paulsen, & others. 1992;54:852–60*
Pavanello M. *see* Bardini, Bonavina, & others. 1992;54:1165–7*
Pavanello M. *see* Bardini, Segalin, & others. 1992;54:576–7,HW
Pawade A, de Leval MR, Elliott MJ, Stark J. Pulmonary artery sling. 1992;54:967–70*
Pearce A. *see* Douville, Kratz, & others. 1992;54:56–61*
Pearl JM, Laks H, Drinkwater DC, Meneshian A, Martin SM, Curzan M, Chang PA. Fluosol cardioplegia results in complete functional recovery: a comparison with blood cardioplegia. 1992;54:1144–50*
Pearl JM. *see* Laks, Gates, & others. 1992;54:169–72,HW
Pearson PJ, Evora PRB, Schaff HV. Bioassay of EDRF from internal mammary arteries: implications for early and late bypass graft patency. 1992;54:1078–84*
Peigh PS. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Pellegrini DP, Mucci SJ, Durzinsky DS, Chaudhuri PK. Placement of an endotracheal tube in the short tracheal stump. 1992;54:578–9,HW
Pennington DG. *see* Fiore, Naunheim, & others. 1992;54:68–73*
Pennington DG. *see* Lohmann, McBride, & others. 1992;54:1226–7,HW
Pepper JR. *see* Kallis, Sneddon, & others. 1992;54:1182–5*
Pera M, Trastek VF, Carpenter HA, Allen MS, Deschamps C, Pairolero PC. Barrett's esophagus with high-grade dysplasia: an indication for esophagectomy? 1992;54:199–204*
Peracchia A. *see* Bardini, Bonavina, & others. 1992;54:1165–7*
Peracchia A. *see* Bardini, Segalin, & others. 1992;54:576–7,HW
Perez G. *see* Menasché, Peynet, & others. 1992;54:472–8*
Perez I. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Perez-Atayde A. *see* Shamberger, Wohl, & others. 1992;54:1206–8,CR
Peynet J. *see* Menasché, Peynet, & others. 1992;54:472–8*
Pfister AJ, Zaki MS, Garcia JM, Mispireta LA, Corso PJ, Qazi AG, Boyce SW, Coughlin TR Jr, Gurny P. Coronary artery bypass without cardiopulmonary bypass. 1992;54:1085–92*
Phillips SJ, Zeff RH, Kongtahworn C, Grignon A, Barker L, Iannone LA, Tannenbaum M, Verhey MH, Wickemeyer WJ, Ghali MG, Gordon DF. Benefits of combined balloon pumping and percutaneous cardiopulmonary bypass. 1992;54:908–10*
Phillips WS. *see* Burton, Phillips, & others. 1992;54:1019–20,CP
Piccione W Jr. *see* Wilson, Ilbawi, & others. 1992;54:892–3*
Piehler JM. *see* Borkon, Failing, & others. 1992;54:884–91*
Pin I. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Pison C. *see* Brichon, Blin, & others. 1992;54:777–8,CR
Piwnica A. *see* Menasché, Fleury, & Piwnica. 1992;54:392–3,UP
Piwnica A. *see* Menasché, Peynet, & others. 1992;54:472–8*
Piwnica A. *see* Muehrcke, Daggett, & others. 1992;54:876–83,DI
Pochettino A. *see* Hooper, Niinami, & others. 1992;54:316–22*
Pogrebniak HW, Haas G, Linehan WM, Rosenberg SA, Pass HI. Renal cell carcinoma: resection of solitary and multiple metastases. 1992;54:33–8*
Poirier NL. *see* Morin, Hedderich, & others. 1992;54:911–4*
Pokela R. *see* Juvonen, Lepojärvi, & others. 1992;54:560–1,CR
Pond CG. *see* Heerdt, Pond, & others. 1992;54:959–66*
Pornviliwan S. *see* Karl, Sano, & others. 1992;54:903–7*
Portoghese M. *see* Acar, Jebara, & others. 1992;54:652–60*
Portoghese M. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Portogues CG. *see* Horowitz, Portogues, & others. 1992;54:782–3,CR
Pouard P. *see* Vouhé, Tamisier, & others. 1992;54:621–7*
Poulton TJ. Visualization of coronary artery anastomoses by gas jet. 1992;54:598–9,CP
Prabhakar G. *see* Kumar, Prabhakar, & others. 1992;54:797–9,HW
Prabhakar G. *see* Kumar, Prabhakar, & others. 1992;54:989–90,CR

Präuer H-W. *see* Müller, Salzer, & others. 1992;54:493–7*

Pridjian AK, Tacy TA, Teske D, Bove EL. Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease. 1992;54:355–6,CR

Pridjian AK. *see* Lupinetti, Pridjian, & others. 1992;54:467–71*

Prior C. *see* Müller, Salzer, & others. 1992;54:493–7*

Putnam JB Jr. *see* Cybulsky, Lanza, & others. 1992;54:533–7*

Putnam JB Jr. *see* Lanza, Natarajan, & others. 1992;54:244–8*

Putnam JB Jr. *see* Pogrebniak, Haas, & others. 1992;54:33–8,DI

Qazi AG. *see* Pfister, Zaki, & others. 1992;54:1085–92*

Quaegebeur JM. *see* Lupinetti, Pridjian, & others. 1992;54:467–71,DI

Quaegebeur JM. *see* Vouhé, Tamisier, & others. 1992;54:621–7,DI

Quentin P. *see* Girard, Quentin, & others. 1992;54:259–63*

Rabasa JM. *see* Bernal, Rabasa, & others. 1992;54:152–4,CR

Rabasa JM. *see* Bernal, Rabasa, & Revuelta. 1992;54:816,CP

Radovancevic B. *see* Baldwin, Klima, & others. 1992;54:978–9,CR

Raffa H; Al-Ibrahim K, Kayali MT, Sorefan AA, Rustom M. Central cyanosis due to prominence of the eustachian and thebesian valves. 1992;54:159–60,CR

Rainer WG. Profound hypothermia and circulatory arrest. Reply. 1992;54:596,CP

Rajii-Khorasani A. *see* Maughan, Mohan, & others. 1992;54:818–25,DI

Rakovec P, Brecelj A, Zupan I. Complete cure after a seemingly unsuccessful operation for Wolff-Parkinson-White syndrome. 1992;54:1203–5,CR

Rakowski H. *see* Hsieh, Mishkel, & others. 1992;54:104–10*

Rao KM. *see* Satyanarayana, Rao, & others. 1992;54:810,CP

Rao KS. *see* Satyanarayana, Rao, & others. 1992;54:810,CP

Rao PS, Chopra PS. Balloon angioplasty in the treatment of aortic coarctation. Reply. 1992;54:600–2,CP

Rao PSR. *see* Satyanarayana, Rao, & others. 1992;54:810,CP

Rashad MN. *see* Jones, Izzat, & others. 1992;54:44–9*

Razzouk AJ, Gow R, Finley J, Murphy D, Williams WG. Surgically created Wolff-Parkinson-White syndrome after Fontan operation. 1992;54:974–7,CR

Reddy KV. *see* Satyanarayana, Rao, & others. 1992;54:810,CP

Reed GE. *see* Dzik, Fleisher, & others. 1992;54:1177–81*

Reed MK, Iverson LIG. Simplified correction of outflow obstruction after mitral valve replacement. 1992;54:985–6,CR

Reed WA. *see* Borkon, Failing, & others. 1992;54:884–91*

Rees A. *see* Citak, Rees, & Mavroudis. 1992;54:755–60*

Rees GM. *see* John, Edmondson, & Rees. 1992;54:190,CP

Registry of the International Society for Heart Lung Transplantation. *see* Karwande, Ensley, & others. 1992;54:840–5*

Regnard J-F. *see* Icard, Regnard, & others. 1992;54:99–103*

Reid AW. *see* Dimitri & Reid. 1992;54:395,CP

Reitz BA. *see* Boglioli, Traill, & others. 1992;54:1209–11,CR

Renlund DG. *see* Karwande, Ensley, & others. 1992;54:840–5*

Renlund DG. *see* Karwande, Renlund, & others. 1992;54:1039–45*

Reul GJ. *see* Fernandes, Kadivar, & others. 1992;54:732–40*

Revuelta JM. *see* Bernal, Rabasa, & others. 1992;54:152–4,CR

Revuelta JM. *see* Bernal, Rabasa, & Revuelta. 1992;54:816,CP

Rice TW. *see* Daniel, Fleischer, & others. 1992;54:686–90,DI

Richenbacher WE. *see* Karwande, Ensley, & others. 1992;54:840–5*

Richenbacher WE. *see* Karwande, Renlund, & others. 1992;54:1039–45*

Ricketts RR. *see* Symbas, Justicz, & Ricketts. 1992;54:177–83,CT

Ridley PD, Khaghani A, Musumeci F, Favaloro R, Akl E-S, Banner NR, Mitchell AG, Yacoub MH. Heterotopic heart transplantation and recipient heart operation in ischemic heart disease. 1992;54:333–7*

Ringel RE. *see* Laschinger, Ringel, & others. 1992;54:371–3,CR

Rizzo RJ, Whittemore AD, Couper GS, Donaldson MC, Aranki SF, Collins JJ Jr, Mannick JA, Cohn LH. Combined carotid and coronary revascularization: the preferred approach to the severe vasculopath. 1992;54:1099–109*

Robicsek F. *see* Creswell, Rosenbloom, & others. 1992;54:11–20,DI

Rodgers BM. *see* Cummings, Wyatt, & others. 1992;54:276–8*

Roeslin N. *see* Massard, Roeslin, & others. 1992;54:1159–64*

Rohman M. *see* Ivatury & Rohman. 1992;54:1247–8,CP

Rojas-Miranda A. *see* Icard, Regnard, & others. 1992;54:99–103*

Romano M. *see* Le Houerou, Singh, & others. 1992;54:815–6,CP

Romero LH. *see* Landreneau, Hazelrigg, & others. 1992;54:415–20,DI

Romero LH. *see* Mack, Aronoff, & others. 1992;54:403–9,DI

Ronquist G. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*

Roques XF. *see* Couraud, Baudet, & others. 1992;54:397,CP

Rosenberg SA. *see* Pogrebniak, Haas, & others. 1992;54:33–8*

Rosenbloom M. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*

Rosenbloom M. *see* Heerdt, Pond, & others. 1992;54:959–66*

Rosenkranz ER, Murphy DJ Jr, Cosgrove DM III. Surgical management of left coronary artery ostial atresia and supravalvar aortic stenosis. 1992;54:779–81,CR

Ross D. Ross' first homograft replacement of the aortic valve. Reply. 1992;54:810,CP

Rossi NP. Role of open lung biopsy in diagnosing pulmonary complications of AIDS. 1992;54:902,IC

Roth JA. *see* Cybulsky, Lanza, & others. 1992;54:533–7*

Roth JA. *see* Lanza, Natarajan, & others. 1992;54:244–8*

Rowles JR. *see* Karwande & Rowles. 1992;54:164–5,HW

Rowles JR. *see* Karwande & Rowles. 1992;54:791–3,HW

Ruffcorn M. *see* Davies, Wells, & others. 1992;54:1020,CP

Ruggiero R. *see* Hooper, Niinami, & others. 1992;54:316–22*

Ruol A. *see* Bardini, Segalin, & others. 1992;54:576–7,HW

Rusch VW. *see* Burt, Fulton, & others. 1992;54:226–32*

Rusch VW. *see* Martini, Burt, & others. 1992;54:460–6*

Rustom M. *see* Raffa, Al-Ibrahim, & others. 1992;54:159–60,CR

Ryan MB. *see* Cybulsky, Lanza, & others. 1992;54:533–7*

Ryan WH. *see* Mack, Aronoff, & others. 1992;54:403–9*

Sade RM. *see* Kratz, Gillette, & others. 1992;54:485–9*

Sade RM. *see* Ungerleider, Greeley, & others. 1992;54:691–8,DI

Sade RM. *see* Warren, Heath, & Brand. 1992;54:240–3,DI

Sadeghi AM. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*

Sadler R. *see* Davies, Wells, & others. 1992;54:1020,CP

Safi HJ. *see* Svensson, Crawford, & others. 1992;54:427–39*

Saha SP. *see* Harpole, Feldman, & others. 1992;54:50–5,DI

Sakai T. *see* Okita, Miki, & others. 1992;54:771–3,CR

Sako EY. A Textbook of Cardioplegia for Difficult Clinical Problems, edited by Richard M. Engelman, MD, and Sidney Levitsky, MD. 1992;54:994,RV

Saksena DS. *see* Cosgrove, Heric, & others. 1992;54:1031–8,DI

Sakurai M. *see* Satoh, Kobayashi, & others. 1992;54:794–6,HW

Salerno G. *see* Graffigna, Vigano, & others. 1992;54:338–43*

Salerno J. *see* Graffigna, Pagani, & others. 1992;54:1093–8*

Salerno TA, Teoh KHT. Visualization of coronary artery anastomoses by gas jet. Reply. 1992;54:599,CP

Salerno TA. *see* Christakis, Koch, & others. 1992;54:449–59*

Salerno TA. *see* Panos, Ali, & others. 1992;54:1137–8*

Salerno TA. *see* Panos, Teoh, & others. 1992;54:555–6,CR

Salzer GM. *see* Müller, Salzer, & others. 1992;54:493–7*

Sampalis J. *see* Morin, Hedderich, & others. 1992;54:911–4*
Sampathkumar A. Hemodynamic effects of pericardial closure. 1992;54:1023,CP
Sampathkumar A. Extended approach to the mitral valve. 1992; 54:596–7,CP
Sandhu R. *see* Feindel, Sandhu, & others. 1992;54:1120–5*
Sano S. *see* Karl, Sano, & others. 1992;54:903–7*
Sanofsky SJ. *see* Singh, Feng, & Sanofsky. 1992;54:538–40*
Sarkis A. *see* Jebara, Chauvaud, & others. 1992;54:323–6*
Sato K. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW
Sato N. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW
Sato T. *see* Hisatomi, Isomura, & others. 1992;54:271–5*
Sato T. *see* Tamiya, Yamashiro, & others. 1992;54:717–24*
Satoh H, Kobayashi T, Hiraishi T, Sakurai M, Fudemoto Y, Kaneko M, Nakano S, Matsuda H. New side-holed sheath for intraaortic balloon pumping to maintain limb perfusion. 1992;54:794–6,HW
Satyanarayana PV, Rao PSR, Rao KM, Chandra AS, Rao KS, Reddy KV. Continuous normothermic blood cardioplegia: simplified delivery circuit. 1992;54:810,CP
Saunders NR. *see* Mitchell, Saunders, & others. 1992;54:814,CP
Sawada M. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*
Schäfers H-J. *see* Hirt, Haverich, & others. 1992;54:676–80*
Schaff HV. *see* Pearson, Evora, & Schaff. 1992;54:1078–84*
Schlag PN. *see* Machens, Mechtersheimer, & others. 1992;54:774–6,CR
Schmelzer V. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*
Schmidt CA, Wood MN, Vyhmeister EE. Pericardioplasty. 1992; 54:584–5,HW
Schneider A. *see* Van Raemdonck, Schneider, & Ginsberg. 1992; 54:999–1013,CV
Schoevaerdts J-C. *see* Buche, Schroeder, & others. 1992;54:381–3,HW
Schofield PM. *see* Dunning, Kendall, & others. 1992;54:571–2,CR
Scholz PM. *see* Ting, Nosher, & others. 1992;54:357–8,CR
Schönberger JPAM, Everts PAM, Ercan H, Bredée JJ, Bavinck JH, Berreklouw E, Wildevuur CRM. Low-dose aprotinin in internal mammary artery bypass operations contributes to important blood saving. 1992;54:1172–6*
Schoof P, van Suylen RJ, Bos E. Homograft root replacement for juvenile rheumatoid aortic valve incompetence. 1992;54: 602,CP
Schreinemakers HHJ, De Leyn PRJ, Marcus M, Wouters P, Moerman PLE, Flameng W, Lerut T, Cooper JD. Role of the bronchial arteries in lung function. Reply. 1992;54:396–7,CP
Schroeder E. *see* Buche, Schroeder, & others. 1992;54:381–3,HW
Schurek JO. *see* Odell, Schurek, & others. 1992;54:283–5*
Schwalb H. *see* Karck, Vivi, & others. 1992;54:348–51*
Schwartz DS. *see* Blitz, McLoughlin, & others. 1992;54:364–5,CR
Sealy WC, Kopelman HE, Murphy DA. Accessory atrioventricular node and bundle: a cause of antidromic reentry tachycardia. 1992;54:306–10*
Sears JJ. *see* Kern, Morana, & others. 1992;54:541–6*
Segalin A. *see* Bardini, Segalin, & others. 1992;54:576–7,HW
Seidenberg J. *see* Ziemer, Heinemann, & others. 1992;54:971–3,CR
Seifert PE. *see* Hazelrigg, Auer, & Seifert. 1992;54:528–32*
Seifert PE. *see* Hill, Bruhn, & others. 1992;54:699–704*
Sekela ME, Smart FW, Noon GP, Young JB. Attenuation of waiting time mortality with heterotopic heart transplantation. 1992;54:547–52*
Sendegeya SZ. *see* Sharpe, Sendegeya, & others. 1992;54:366–7,CR
Serrick C. *see* Adoumie, Serrick, & others. 1992;54:1071–7*
Sett SS. *see* Webber, Sett, & LeBlanc. 1992;54:344–7*
Shah SS, Thompson J, Goldstraw P. Results of operation without adjuvant therapy in the treatment of small cell lung cancer. 1992;54:498–501*
Shahian DM. Retrograde coronary sinus cardioplegia in the presence of persistent left superior vena cava. 1992;54: 1214–5,CR
Shahian DM, Williamson WA, Streitz JM Jr, Venditti FJ. Subfascial implantation of implantable cardioverter defibrillator generator. 1992;54:173–4,HW
Shaikh SS. *see* Chechani, Landreneau, & Shaikh. 1992;54:296–300*
Shamberger RC, Wohl ME, Perez-Atayde A, Hendren WH. Pneumatocele complicating hyperimmunoglobulin E syndrome (Job's syndrome). 1992;54:1206–8,CR
Sharma BK, Calderon M, Ott DA. Coarctation repair in neonates with subclavian-sparing advancement flap. 1992;54:137–41*
Sharpe DAC, Sendegeya SZ, Parry DH, Drakeley MJ. Tracheoesophageal fistula after chemotherapy for lymphoma. 1992;54:366–7,CR
Shaw RR. *see* Harpole, Feldman, & others. 1992;54:50–5,DI
Sheiner NM. *see* Bégin & Sheiner. 1992;54:564–5,CR
Shemin RJ. *see* Aldea, Connelly, & others. 1992;54:789–90,HW
Shennib H, Noirclerc M, Ernst P, Metras D, Mulder DS, Giudicelli R, Lebel F, Dumon J-F, Cystic Fibrosis Transplant Study Group. Double-lung transplantation for cystic fibrosis. 1992;54:27–32*
Shennib H. *see* Adoumie, Serrick, & others. 1992;54:1071–7*
Shennib H. *see* Spray, Mallory, & others. 1992;54:216–25,DI
Shiang HH. *see* Mezrow, Sadeghi, & others. 1992;54:609–16*
Shibata Y. *see* Watanabe, Fuse, & others. 1992;54:479–84*
Shuman TS. *see* Hogue, Barzilai, & others. 1992;54:562–3,CR
Shumway SJ. *see* Irwin, Bianco, & others. 1992;54:669–75*
Sidi D. *see* Vouhé, Tamisier, & others. 1992;54:621–7*
Siegman MG, Anderson RV, Balaban RS, Ceckler TL, Clark RE, Swain JA. Barbiturates impair cerebral metabolism during hypothermic circulatory arrest. 1992;54:1131–6*
Siegman MG. *see* Anderson, Siegman, & others. 1992;54:1126–30*
Siewert JR. *see* Liebermann-Meffert, Meier, & Siewert. 1992;54: 1110–5*
Simberkoff MS. *see* Bräu, Esposito, & Simberkoff. 1992;54:552–4,CR
Simpson IA. *see* Kallis, Sneddon, & others. 1992;54:1182–5*
Simpson KA. *see* Furnary, Magovern, & others. 1992;54:1139–43*
Simpson KA. *see* Furnary, Magovern, & others. 1992;54:233–9*
Sinclair L. *see* Christakis, Koch, & others. 1992;54:449–59*
Singh AI. *see* Le Houerou, Singh, & others. 1992;54:815–6,CP
Singh AK, Feng WC, Sanofsky SJ. Long-term results of St. Jude medical valve in the tricuspid position. 1992;54:538–40*
Sirivella S, Gielchinsky I, Parsonnet V. Modified technique of internal mammary artery harvest. 1992;54:190,CP
Sisler GE. *see* Crawford, Galloway, & others. 1992;54:212–5,DI
Sisler GE. *see* Lewis, Caccavale, & others. 1992;54:421–6*
Sisler GE. *see* Lewis, Sisler, & Caccavale. 1992;54:80–3*
Sisler GE. *see* Miller, Allen, & others. 1992;54:410–4,DI
Sisto DA, Hoffman DM, Fernandes S, Frater RWM. Is use of the intraaortic balloon pump in octogenarians justified? 1992; 54:507–11*
Skinner DB. *see* Pera, Trastek, & others. 1992;54:199–204,DI
Skotnicki SH. *see* van Son, Skotnicki, & others. 1992;54:130–3*
Slovut DP. *see* Irwin, Bianco, & others. 1992;54:669–75*
Smart FW. *see* Sekela, Smart, & others. 1992;54:547–52*
Smith CR. *see* Adoumie, Serrick, & others. 1992;54:1071–7,DI
Smith CR. *see* Laub, Muralidharan, & others. 1992;54:826–31,DI

Smith EEJ. *see* Kallis, Sneddon, & others. 1992;54:1182–5*

Smith F. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR

Smith JA, Goldstein J. Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis. 1992;54:766–8,CR

Smith PK. *see* Pearson, Evora, & Schaff. 1992;54:1078–84,DI

Sneddon JF. *see* Kallis, Sneddon, & others. 1992;54:1182–5*

Snow NJ. *see* Douville, Kratz, & others. 1992;54:56–61,DI

Sokil AB. *see* Kaplan, Weiman, & others. 1992;54:374–5,HW

Sorefan AA. *see* Raffa, Al-Ibrahim, & others. 1992;54:159–60,CR

Southard JH. *see* Stringham, Paulsen, & others. 1992;54:852–60*

Soutter DI. *see* Birnbaum, Lichtenstein, & others. 1992;54:987–8,CR

Spampinato N. *see* Golino, Stassano, & Spampinato. 1992;54:1246–7,CP

Spence PA, Lust RM, Zeri RS, Jolly SR, Mehta PM, Otaki M, Sun YS, Chitwood WR Jr. Competitive flow from a fully patent coronary artery does not limit acute mammary graft flow. 1992;54:21–6*

Spencer FC. *see* Crawford, Galloway, & others. 1992;54:212–5*

Spiess BD. Thromboelastogram and postoperative hemorrhage. 1992;54:810–1,CP

Spinale FG. *see* Douville, Kratz, & others. 1992;54:56–61*

Spodick DH. Pericardial window. Reply. 1992;54:192,CP

Spotnitz AJ. *see* Ting, Nosher, & others. 1992;54:357–8,CR

Spotnitz WD. *see* Cummings, Wyatt, & others. 1992;54:276–8*

Spray TL, Mallory GB, Canter CE, Huddleston CB, Kaiser LR. Pediatric lung transplantation for pulmonary hypertension and congenital heart disease. 1992;54:216–25*

Spray TL. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*

Spray TL. *see* Ungerleider, Greeley, & others. 1992;54:691–8,DI

Spray TL. *see* Ziomek, Harrell, & others. 1992;54:861–8,DI

Spritzer CE. *see* Glower, Bashore, & Spritzer. 1992;54:368–70,CR

Stacchino C. *see* Casabona, De Paulis, & others. 1992;54:681–5*

Stark JF. *see* Lupinetti, Pridjian, & others. 1992;54:467–71,DI

Stark JF. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75,DI

Stark J. *see* Pawade, de Leval, & others. 1992;54:967–70*

Starnes VA. *see* Griffith, Hardesty, & others. 1992;54:846–51,DI

Starnes VA. *see* Spray, Mallory, & others. 1992;54:216–25,DI

Starzl TE. *see* Armitage, Kormos, & others. 1992;54:205–11*

Stassano P. *see* Golino, Stassano, & Spampinato. 1992;54:1246–7,CP

Stein B. *see* McLean, Svensson, & others. 1992;54:894–7*

Stephenson LW. *see* Hooper, Niinami, & others. 1992;54:316–22*

Steven JM. *see* Jobes, Nicolson, & others. 1992;54:150–1,CR

Stewart RW. *see* Cosgrove, Heric, & others. 1992;54:1031–8*

Stewart RW. *see* Golding, Crouch, & others. 1992;54:1059–64*

Strauss G. *see* Sugarbaker, Mentzer, & Strauss. 1992;54:941–6*

Streitz JM Jr, Williamson WA, Ellis FH Jr. Current concepts concerning the nature and treatment of Barrett's esophagus and its complications. 1992;54:586–91,CV

Streitz JM Jr. *see* Shahian, Williamson, & others. 1992;54:173–4,HW

Stringham JC, Paulsen KL, Southard JH, Fields BL, Belzer FO. Improved myocardial ischemic tolerance by contractile inhibition with 2,3-butanedione monoxime. 1992;54:852–60*

Su Z-K. *see* Liu, Su, & Ding. 1992;54:1196–202*

Suemasu K. *see* Asamura, Goya, & others. 1992;54:147–9,CR

Suen HC. *see* Grillo, Suen, & others. 1992;54:3–10*

Suenaga Y. *see* Watanabe, Abe, & others. 1992;54:993–4,HW

Sugarbaker DJ, Mentzer SJ, Strauss G. Extrapleural pneumonectomy in the treatment of malignant pleural mesothelioma. 1992;54:941–6*

Sugawara M-A. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW

Suma H. Length of the in situ right gastroepiploic artery for coronary artery bypass. Reply. 1992;54:1245,CP

Sun YS. *see* Spence, Lust, & others. 1992;54:21–6*

Sun Z. *see* David, Armstrong, & Sun. 1992;54:661–8*

Suttorp MJ. *see* van Heurn, Hamerlijnck, & others. 1992;54:157–8,CR

Suzuki S. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*

Svennevig JL. *see* Videm, Fosse, & others. 1992;54:725–31*

Svensson LG. Approach for insertion of aortic composite valve grafts. 1992;54:376–8,HW

Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Composite valve graft replacement of the proximal aorta: comparison of techniques in 348 patients. 1992;54:427–39*

Svensson LG, Crawford ES, Patel V, McLean TR, Jones JW, DeBakey ME. Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping. 1992;54:74–9*

Svensson LG. *see* Jones, Izzat, & others. 1992;54:44–9*

Svensson LG. *see* Maughan, Mohan, & others. 1992;54:818–25,DI

Svensson LG. *see* McLean, Svensson, & others. 1992;54:894–7*

Swain JA. *see* Anderson, Siegman, & others. 1992;54:1126–30*

Swain JA. *see* Siegman, Anderson, & others. 1992;54:1131–6*

Swartz MT. *see* Lohmann, McBride, & others. 1992;54:1226–7,HW

Sweeney MS, Frazier OH. Device-supported myocardial revascularization: safe help for sick hearts. 1992;54:1065–70*

Symbas PN, Justicz AG, Ricketts RR. Rupture of the airways from blunt trauma: treatment of complex injuries. 1992;54:177–83,CT

Symes JF. *see* Morin, Hedderich, & others. 1992;54:911–4*

Syohji Y. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*

Szentpetery S. Management of aortic cannulation site blowouts. 1992;54:582–3,HW

Tabayashi K, Ohmi M, Syohji Y, Akimoto H, Matuki K, Turu Y, Mohri H. Thoracic aortic operations in patients aged 70 years or older. 1992;54:279–82*

Tacy TA. *see* Pridjian, Tacy, & others. 1992;54:355–6,CR

Tahata T. *see* Okita, Miki, & others. 1992;54:771–3,CR

Taillefer R. *see* Topart, Deschamps, & others. 1992;54:1046–52*

Takahashi S. *see* Takeuchi, Suzuki, & others. 1992;54:327–32*

Takeuchi K, Suzuki S, Kako N, Kobayashi M, Takahashi S, Sawada M, Honma T, Iwabuchi S, Fukui K, Koyama K, Koie H. A prostacyclin analogue reduces free radical generation in heart-lung transplantation. 1992;54:327–32*

Talenti E. *see* Bortolotti, Ius, & others. 1992;54:952–8*

Tamai S. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR

Tamisier D. *see* Vouhé, Tamisier, & others. 1992;54:621–7*

Tamiya T, Yamashiro T, Hata A, Kuge K, Asano S, Sato T. Electrophysiologic study of dysrhythmias after atrial operations in dogs. 1992;54:717–24*

Tanaka M. *see* Watanabe, Abe, & others. 1992;54:993–4,HW

Tanaka S. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR

Tannenbaum M. *see* Phillips, Zeff, & others. 1992;54:908–10*

Tassini M. *see* Karck, Vivi, & others. 1992;54:348–51*

Tatebe S, Eguchi S, Miyamura H, Nakazawa S, Watanabe H, Sugawara M-A, Hayashi J-I, Date K, Nakagawa S. Limited vertical skin incision for median sternotomy. 1992;54:787–8,HW

Tatebe S, Nakazawa M, Miyamura H, Hayashi J-I, Eguchi S, Imai S. Myocardial protection of neonatal heart by cardioplegic solution with recombinant human superoxide dismutase. 1992;54:124–9*

Tatsumi A. *see* Okita, Miki, & others. 1992;54:771–3,CR

Tavilla G. Length of the in situ right gastroepiploic artery for coronary artery bypass. 1992;54:1244–5,CP
Taylor KM. *see* Cosgrove, Heric, & others. 1992;54:1031–8,DI
Taylor KM. *see* Efstratiadis, Munsch, & others. 1992;54:1022–3,CP
Taylor PC. *see* Cosgrove, Heric, & others. 1992;54:1031–8*
Taylor PC. *see* Golding, Crouch, & others. 1992;54:1059–64*
Tchervenkov CI. *see* Ergina & Tchervenkov. 1992;54:599–600,CP
Tedder M, Anstadt MP, Tedder SD, Lowe JE. Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy. 1992;54:387–91,CV
Tedder SD. *see* Tedder, Anstadt, & others. 1992;54:387–91,CV
Teoh KHT. *see* Salerno & Teoh. 1992;54:599,CP
Teoh KT. *see* Panos, Teoh, & others. 1992;54:555–6,CR
Teoh N. *see* Alvarez, Teoh, & Deal. 1992;54:1229–30,HW
Teske D. *see* Pridjian, Tacy, & others. 1992;54:355–6,CR
Tewari P, Kumar M. Acute pulmonary edema in closed mitral commissurotomy. 1992;54:191,CP
Theodore P. *see* Kron, Kern, & others. 1992;54:617–20*
Thiene G. *see* Bortolotti, Ius, & others. 1992;54:952–8*
Thompson J. *see* Shah, Thompson, & Goldstraw. 1992;54:498–501*
Thornby JI. *see* Jones, Izzat, & others. 1992;54:44–9*
Thornby JI. *see* McLean, Svensson, & others. 1992;54:894–7*
Thurer RL. Safety and efficacy of autologous blood donation before elective aortic valve operation. 1992;54:1180–1,IC
Tietjen PA. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR
Ting W, Nosher JL, Scholz PM, Spotnitz AJ. Bilateral adrenal hemorrhage after an open heart operation. 1992;54:357–8,CR
Titrator Multicenter Study Group. *see* Chitwood, Cosgrove, & others. 1992;54:517–22*
Tobe S. *see* Yamashita, Nakamura, & others. 1992;54:761–3,CR
Tobe S. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Todd JC. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*
Todd TRJ. *see* Burt, Fulton, & others. 1992;54:226–32,DI
Todd TRJ. *see* Martini, Burt, & others. 1992;54:460–6,DI
Todd TRJ. *see* Miller, Allen, & others. 1992;54:410–4,DI
Tofukuji M. *see* Ohmi, Tofukuji, & others. 1992;54:1223–5,HW
Toms J. *see* Ho, Gerlis, & others. 1992;54:264–70*
Topart P, Deschamps C, Taillefer R, Duranceau A. Long-term effect of total fundoplication on the myotomized esophagus. 1992;54:1046–52*
Torres AR. *see* Dietl & Torres. 1992;54:580–1,HW
Touchot B. *see* Menasché, Peynet, & others. 1992;54:472–8*
Townsend ER. *see* Gaer, Tsang, & others. 1992;54:512–6*
Townsend ER. *see* Liakakos, Ohri, & others. 1992;54:814,CP
Townsend ER. *see* Patel, Townsend, & Fountain. 1992;54:84–8*
Trachiotis GD, Hafner GH, Hix WR, Aaron BL. Role of open lung biopsy in diagnosing pulmonary complications of AIDS. 1992;54:898–902*
Traill TA. *see* Boglioli, Traill, & others. 1992;54:1209–11,CR
Trastek VF. *see* Miller, Allen, & others. 1992;54:410–4*
Trastek VF. *see* Pera, Trastek, & others. 1992;54:199–204*
Treasure T. *see* Kallis, Treasure, & others. 1992;54:741–3*
Tribble CG. *see* Cummings, Wyatt, & others. 1992;54:276–8*
Tribble CG. *see* Daniel, Fleischer, & others. 1992;54:686–90*
Trulock EP. *see* Haydock, Low, & others. 1992;54:1189–92*
Tsang V. *see* Gaer, Tsang, & others. 1992;54:512–6*
Tsuchida K, Hashimoto A, Endo M, Koyanagi H. Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation. 1992;54:161–3,CR
Tsuchiya R. *see* Asamura, Goya, & others. 1992;54:147–9,CR
Tsuji F. *see* Yamashita, Oobo, & others. 1992;54:921–4*
Tubeszewski K. *see* Wilson, Ilbawi, & others. 1992;54:892–3*
Tuman KJ, McCarthy RJ, Ivankovich AD. Thromboelastogram and postoperative hemorrhage. 1992;54:811–2,CP
Turina MI. *see* Carrel, Linka, & Turina. 1992;54:352–4,CR
Turu Y. *see* Tabayashi, Ohmi, & others. 1992;54:279–82*
Tydén H. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*

Ueda Y. *see* Okita, Miki, & others. 1992;54:771–3,CR
Uemura H. *see* Matsuki, Yagihara, & others. 1992;54:991–2,HW
Ulicny KS Jr, Schmelzer V, Flege JB Jr, Todd JC, Mitts DL, Melvin DB, Wright CB. Concomitant cardiac and pulmonary operation: the role of cardiopulmonary bypass. 1992;54:289–95*
Ungerleider RM, Greeley WJ, Kanter RJ, Kisslo JA. The learning curve for intraoperative echocardiography during congenital heart surgery. 1992;54:691–8*
Ungerleider RM. *see* Mezrow, Sadeghi, & others. 1992;54:609–16,DI
Unruh HW. Vascular and interstitial effect of University of Wisconsin solution on canine lung. 1992;54:1168–71*
Uretzky G. *see* Karck, Vivi, & others. 1992;54:348–51*
Uriuda Y. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR
Uva MS, Jebara VA, Acar C, Dervanian P, Chauvaud S, Fuzellier JF, Fabiani J-N, Deloche A, Carpentier AF. Mitral valve repair in patients with endomyocardial fibrosis. 1992;54:89–92*
Uva MS. *see* Jebara, Chauvaud, & others. 1992;54:323–6*

Vahdat O. *see* Defraigne, Vahdat, & others. 1992;54:983–4,CR
Valente M. *see* Bortolotti, Ius, & others. 1992;54:952–8*
Valfrè C. *see* Bortolotti, Ius, & others. 1992;54:952–8*
Vallieres E. *see* Couraud, Baudet, & others. 1992;54:397,CP
van Asten WNJC. *see* van Son, Skotnicki, & others. 1992;54:130–3*
van der Linden J. *see* Wesslén, van der Linden, & others. 1992;54:1151–8*
van der Merwe PL. *see* Knott-Craig, van der Merwe, & others. 1992;54:557–9,CR
Van Devanter SH. *see* Ziomek, Harrell, & others. 1992;54:861–8*
van Heurn LWE, Hamerlijnck RPHM, de la Rivière AB, Suttorp MJ, Ernst SMPG, Vermeulen FEE. Combined traumatic avulsion of the aortic valve and rupture of the left common carotid artery. 1992;54:157–8,CR
van Oeveren W. *see* Jansen, van Oeveren, & others. 1992;54:744–8*
Van Raemdonck DE, Schneider A, Ginsberg RJ. Surgical treatment for higher stage non–small cell lung cancer. 1992;54:999–1013,CV
van Son JAM, Skotnicki SH, Folmer HA, van Asten WNJC. Reactive hyperemia in the nonused internal mammary artery after median sternotomy. 1992;54:130–3*
van Suylen RJ. *see* Schoof, van Suylen, & Bos. 1992;54:602,CP
van Vliet MH. *see* Jansen, van Oeveren, & others. 1992;54:744–8*
Velly J-F. *see* Couraud, Baudet, & others. 1992;54:397,CP
Velly J-F. *see* Nashef, Dromer, & others. 1992;54:937–40*
Venditti FJ. *see* Shahian, Williamson, & others. 1992;54:173–4,HW
Ventemiglia RA. Role of the bronchial arteries in lung function. 1992;54:395–6,CP
Verhey MH. *see* Phillips, Zeff, & others. 1992;54:908–10*
Vermeulen FEE. *see* van Heurn, Hamerlijnck, & others. 1992;54:157–8,CR
Vernant F. *see* Vouhé, Tamisier, & others. 1992;54:621–7*
Verrier ED. *see* Menasché, Peynet, & others. 1992;54:472–8,DI
Verrier ED. *see* Spence, Lust, & others. 1992;54:21–6,DI
Vester SR. *see* Faber, Vester, & others. 1992;54:1021–2,CP
Veyssié L. *see* Menasché, Peynet, & others. 1992;54:472–8*

Victor TA. *see* Winchester, Victor, & Fry. 1992;54:145–6,CR

Videm V, Fosse E, Mollnes TE, Garred P, Svennevig JL. Time for new concepts about measurement of complement activation by cardiopulmonary bypass? 1992;54:725–31*

Viganò M. *see* Graffigna, Pagani, & others. 1992;54:1093–8*

Vigano M. *see* Graffigna, Vigano, & others. 1992;54:338–43*

Vivi A. *see* Karck, Vivi, & others. 1992;54:348–51*

Vouhé PR, Tamisier D, Sidi D, Vernant F, Mauriat P, Pouard P, Leca F. Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation. 1992;54:621–7*

Vrandecic MOP. *see* Casabona, De Paulis, & others. 1992;54:681–5*

Vyhmeister EE. *see* Schmidt, Wood, & Vyhmeister. 1992;54:584–5,HW

Wagner I. *see* Carroll, Kramer, & others. 1992;54:1212–3,CR

Wahlers T. *see* Hirt, Haverich, & others. 1992;54:676–80*

Wain JC. *see* Grillo, Suen, & others. 1992;54:3–10*

Wakabayashi A. *see* Miller, Allen, & others. 1992;54:410–4,DI

Waldhausen JA. Coarctation repair in neonates with subclavian-sparing advancement flap. 1992;54:140–1,IC

Waldhausen JA. *see* Myers, McConnell, & Waldhausen. 1992;54:869–75*

Walker DR. *see* Martin, Horkay, & others. 1992;54:812–3,CP

Walley VM, Keon CA, Khalili M, Moher D, Campagna M, Keon WJ. Ionescu-Shiley valve failure I: experience with 125 standard-profile explants. 1992;54:111–6*

Walley VM, Keon CA, Khalili M, Moher D, Campagna M, Keon WJ. Ionescu-Shiley valve failure II: experience with 25 low-profile explants. 1992;54:117–23*

Wang J-S. *see* Lin & Wang. 1992;54:813,CP

Wareing TH. *see* Creswell, Rosenbloom, & others. 1992;54:11–20*

Warren ET, Heath BJ, Brand WW III. A staged expanding pulmonary artery band. 1992;54:240–3*

Warren WH. *see* Faber, Vester, & others. 1992;54:1021–2,CP

Watanabe H. *see* Tatebe, Eguchi, & others. 1992;54:787–8,HW

Watanabe T, Abe T, Tanaka M, Yasuura K, Hikosaka H, Suenaga Y, Hosokawa H. Newly developed holder for a right-angled metal venous cannula. 1992;54:993–4,HW

Watanabe Y, Fuse K, Naruse Y, Kobayashi T, Yamamoto S, Konishi H, Horii T, Shibata Y. Subcutaneous use of erythropoietin in heart surgery. 1992;54:479–84*

Watterson KG, Malm TK, Karl TR, Mee RBB. Absent pulmonary valve syndrome: operation in infants with airway obstruction. 1992;54:1116–9*

Webber SA, Sett SS, LeBlanc JG. Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach. 1992;54:344–7*

Wechsler AS. *see* Stringham, Paulsen, & others. 1992;54:852–60,DI

Weiman DS. *see* Kaplan, Weiman, & others. 1992;54:374–5,HW

Weisel RD. *see* Hsieh, Mishkel, & others. 1992;54:104–10*

Weisel RD. *see* Pearson, Evora, & Schaff. 1992;54:1078–84,DI

Weissberg D. Pericardial window. 1992;54:191,CP

Wekerle T. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR

Wells DG. *see* Davies, Wells, & others. 1992;54:1020,CP

Wesslén O, van der Linden J, Ekroth R, Joachimsson P-O, Nordgren L, Nyström S-O, Ronquist G, Tydén H. Influence of β_1-blockade on myocardial substrates early after a coronary operation. 1992;54:1151–8*

Wessner-Dunlap S. *see* Burt, Fulton, & others. 1992;54:226–32*

Westaby S. Hypothermic thoracic and thoracoabdominal aneurysm operation: a central cannulation technique. 1992;54:253–8*

Wetstein L. Palliative intubation for dysphagia. 1992;54:813–4,CP

Whitman GJR. *see* Kaplan, Weiman, & others. 1992;54:374–5,HW

Whittemore AD. *see* Rizzo, Whittemore, & others. 1992;54:1099–109*

Wickemeyer WJ. *see* Phillips, Zeff, & others. 1992;54:908–10*

Wihlm J-M. *see* Massard, Roeslin, & others. 1992;54:1159–64*

Wildevuur CRH. *see* Jansen, van Oeveren, & others. 1992;54:744–8*

Wildevuur CRM. *see* Schönberger, Everts, & others. 1992;54:1172–6*

Wilken M. *see* Ziemer, Heinemann, & others. 1992;54:971–3,CR

Williams P. *see* Griffith, Hardesty, & others. 1992;54:846–51*

Williams TE Jr. *see* McCaughan, Hawley, & others. 1992;54:705–11*

Williams WG. *see* Razzouk, Gow, & others. 1992;54:974–7,CR

Williamson WA. *see* Shahian, Williamson, & others. 1992;54:173–4,HW

Williamson WA. *see* Streitz, Williamson, & Ellis. 1992;54:586–91,CV

Willman VL. *see* Fiore, Naunheim, & others. 1992;54:68–73*

Wilson GJ. *see* Feindel, Sandhu, & others. 1992;54:1120–5*

Wilson JK. *see* Panos, Teoh, & others. 1992;54:555–6,CR

Wilson N. *see* Kumar, Prabhakar, & others. 1992;54:989–90,CR

Wilson WR Jr, Ilbawi MN, DeLeon SY, Piccione W Jr, Tubeszewski K, Cutilletta AF. Partial median sternotomy for repair of heart defects: a cosmetic approach. 1992;54:892–3*

Winchester DJ, Victor TA, Fry WA. Intercostal hemangioma presenting as a chest wall tumor. 1992;54:145–6,CR

Wisser W. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR

Witz J-P. *see* Massard, Roeslin, & others. 1992;54:1159–64*

Wohl ME. *see* Shamberger, Wohl, & others. 1992;54:1206–8,CR

Wolfe WG. *see* Harpole, Feldman, & others. 1992;54:50–5*

Wolner E. *see* Cosgrove, Heric, & others. 1992;54:1031–8,DI

Wolner E. *see* Oturanlar, Klepetko, & others. 1992;54:1221–2,CR

Wong PS, Goldstraw P. Pulmonary torsion: a questionnaire survey and a survey of the literature. 1992;54:286–8*

Wood MK. Internal mammary artery to lung parenchyma fistula. 1992;54:603,CP

Wood MN. *see* Schmidt, Wood, & Vyhmeister. 1992;54:584–5,HW

Wouters P. *see* Schreinemakers, De Leyn, & others. 1992;54:396–7,CP

Wright CB. *see* Ulicny, Schmelzer, & others. 1992;54:289–95*

Wu M-H, Lai W-W. Aortoesophageal fistula induced by foreign bodies. 1992;54:155–6,CR

Wu M-H. *see* Leu, Chiu, & others. 1992;54:134–6*

Wyatt DA. *see* Cummings, Wyatt, & others. 1992;54:276–8*

Yacoub MH. *see* Gaer, Tsang, & others. 1992;54:512–6*

Yacoub MH. *see* Ridley, Khaghani, & others. 1992;54:333–7*

Yagihara T. *see* Matsuki, Yagihara, & others. 1992;54:991–2,HW

Yamaguchi M. *see* Yoshimura, Yamaguchi, & others. 1992;54:573–5,CR

Yamamoto F. *see* Matsuki, Yagihara, & others. 1992;54:991–2,HW

Yamamoto H. *see* Yamashita, Oobo, & others. 1992;54:921–4*

Yamamoto S. *see* Watanabe, Fuse, & others. 1992;54:479–84*

Yamamoto S. *see* Yamashita, Nakamura, & others. 1992;54:566–8,CR

Yamamoto S. *see* Yamashita, Nakamura, & others. 1992;54:761–3,CR

Yamanda T. *see* Haniuda, Morimoto, & others. 1992;54:311–5*

Yamashiro T. *see* Tamiya, Yamashiro, & others. 1992;54:717–24*

Yamashita C, Nakamura H, Nishikawa Y, Yamamoto S, Okada M, Nakamura K. Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms. 1992;54:566–8,CR

Yamashita C, Nakamura H, Tobe S, Koterazawa T, Yamamoto S. Left ventricular diverticulum with hypertrophy of the left ventricular apex. 1992;54:761–3,CR

Yamashita C, Oobo H, Tsuji F, Tobe S, Yamamoto H, Nakamura H, Okada M, Nakamura K. Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung. 1992;54:921–4*

Yasuda T. *see* Kodama, Doi, & others. 1992;54:1193–5*

Yasuura K. *see* Watanabe, Abe, & others. 1992;54:993–4,HW

Yellin A. *see* Bar-El, Lieberman, & Yellin. 1992;54:995–6,HW

Yokouchi H. *see* Kodama, Doi, & others. 1992;54:1193–5*

Yoshimura N, Yamaguchi M, Oshima Y, Ohashi H, Imai M, Chung H-N, Kyo E. Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries. 1992;54:573–5,CR

Yoshizu H. *see* Haga, Yoshizu, & others. 1992;54:359–60,CR

Young JB. *see* Sekela, Smart, & others. 1992;54:547–52*

Young WG. *see* Harpole, Feldman, & others. 1992;54:50–5*

Yousem SA. *see* Griffith, Hardesty, & others. 1992;54:846–51*

Zaki MS. *see* Pfister, Zaki, & others. 1992;54:1085–92*

Zattera GF. *see* Casabona, De Paulis, & others. 1992;54:681–5*

Zeff RH. *see* Phillips, Zeff, & others. 1992;54:908–10*

Zeigler VL. *see* Kratz, Gillette, & others. 1992;54:485–9*

Zeplin HE. Surgery of aortic dissections with GRF glue. 1992;54:1248–9,CP

Zeri RS. *see* Spence, Lust, & others. 1992;54:21–6*

Ziemer G, Heinemann M, Kaulitz R, Freihorst J, Seidenberg J, Wilken M. Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy. 1992;54:971–3,CR

Ziomek S, Harrell JE Jr, Fasules JW, Faulkner SC, Chipman CW, Moss M, Frazier E, Van Devanter SH. Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation. 1992;54:861–8*

Zupan I. *see* Rakovec, Brecelj, & Zupan. 1992;54:1203–5,CR

Zwischenberger JB. *see* Ziomek, Harrell, & others. 1992;54:861–8,DI

Subject Index
Volume 54 (July–December 1992)

KEY TO ABBREVIATIONS USED FOR ARTICLE CLASSIFICATION

* = Original Article
AN = Announcement
CL = Classics in Thoracic Surgery
CR = Case Report
CP = Correspondence
CT = Collective Review
CV = Current Review
ED = Editorial
HW = How to Do It
KR = Key References
PA = Presidential Address
RE = Report
RV = Review of Recent Books
TR = Tribute
UP = Update

Acadesine
Acadesine (AICA-riboside) improves postischemic cardiac recovery (Bolling, Groh, & others) 1992;54:93–8*
Acidosis
Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest (Anderson, Siegman, & others) 1992;54:1126–30*
Acquired immunodeficiency syndrome
Role of open lung biopsy in diagnosing pulmonary complications of AIDS (Trachiotis, Hafner, & others) 1992;54:898–902*
Treatment of AIDS-related bronchopleural fistula by pleurectomy (Crawford, Galloway, & others) 1992;54:212–5*
Adrenal glands
Bilateral adrenal hemorrhage after an open heart operation (Ting, Nosher, & others) 1992;54:357–8,CR
Adrenergic β-receptor blockade
Influence of β_1-blockade on myocardial substrates early after coronary operation (Wesslén, van der Linden, & others) 1992;54:1151–8*
Age factors
Primary lung cancer in young patients: a study of 82 surgically treated patients (Icard, Regnard, & others) 1992;54:99–103*
Airway
Resectional management of thyroid carcinoma invading the airway (Grillo, Suen, & others) 1992;54:3–10*
Airway obstruction
Absent pulmonary valve syndrome: operation in infants with airway obstruction (Watterson, Malm, & others) 1992;54:1116–9*
Expanding wire stents in benign tracheobronchial disease: indications and complications (Nashef, Dromer, & others) 1992;54:937–40*
Postpneumonectomy syndrome: diagnosis, management, and results (Grillo, Shepard, & others) 1992;54:638–51*
Use of endotracheal silicone stents for relief of tracheobronchial obstruction (Gaer, Tsang, & others) 1992;54:512–6*
The American Association for Thoracic Surgery
Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
Anastomosis, surgical
Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty (Bégin & Sheiner) 1992;54:564–5,CR
Approach for insertion of aortic composite valve grafts (Svensson) 1992;54:376–8,HW
Cervical esophago-esophageal anastomosis (Fraser & Heitmiller) 1992;54:384–6,HW
Extracardiac total cavopulmonary connection (Laschinger, Ringel, & others) 1992;54:371–3,CR
Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW
Technique of open distal anastomosis for repair of descending thoracic aortic aneurysms (Cooley & Baldwin) 1992;54:932–6*
Visualization of coronary artery anastomoses by gas jet (Poulton) 1992;54:598–9,CP; Reply (Salerno & Teoh) 1992;54:599,CP
Aneurysm
Coronary bypass graft aneurysm (Dimitri & Reid) 1992:54;395,CP
Isolated extracardiac unruptured sinus of Valsalva aneurysms (Jebara, Chauvaud, & others) 1992;54:323–6*
Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis (Smith & Goldstein) 1992;54:766–8,CR
True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient (Baldwin, Klima, & others) 1992;54:978–9,CR
Angioplasty
Balloon angioplasty in the treatment of aortic coarctation (Ergina & Tchervenkov) 1992;54:599–600,CP; Reply (Rao & Chopra) 1992;54:600–2,CP
Risk analysis of operative intervention for failed coronary angioplasty (Borkon, Failing, & others) 1992;54:884–91*
Announcement
Thoracic Surgery Foundation for Research and Education (Liddle) 1992;54:595,AN
Aorta
Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation (Vouhé, Tamisier, & others) 1992;54:621–7*
Composite valve graft replacement of the proximal aorta: comparison of techniques in 348 patients (Svensson, Crawford, & others) 1992;54:427–39*
Intrathecal perfusion of an oxygenated perfluorocarbon prevents paraplegia after aortic occlusion (Maughan, Mohan, & others) 1992;54:818–25*
Normothermic cardioplegia: is aortic cross-clamping still synonymous with myocardial ischemia? (Menasché, Peynet, & others) 1992;54:472–8*
Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR

July issue, pp 1–192; August issue, pp 193–400; September issue, pp 401–608; October issue, pp 609–816; November issue, pp 817–1024; December issue, pp 1025–1308.

Aorta (cont'd)
- Safe intraaortic balloon pump placement through the ascending aorta using transesophageal ultrasound (Kaplan, Weiman, & others) 1992;54:374–5,HW
- Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping (Svensson, Crawford, & others) 1992;54:74–9*
- Surgery of aortic dissections with GRF glue (Zeplin) 1992;54:1248–9,CP

Aorta, thoracic
- New surgical technique for type B aortic interruption (Kumar, Prabhakar, & others) 1992;54:797–9,HW
- Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation (Tsuchida, Hashimoto, & others) 1992;54:161–3,CR
- Surgical reconstruction of an ascending aortic dissection in Takayasu's arteritis (Haga, Yoshizu, & others) 1992;54:359–60,CR
- Thoracic aortic operations in patients aged 70 years or older (Tabayashi, Ohmi, & others) 1992;54:279–82*

Aortic aneurysm
- Aneurysm of the ascending aorta after cardiac transplantation (Defraigne, Vahdat, & others) 1992;54:983–4,CR
- Chronic, traumatic pseudoaneurysm of the ascending aorta (Albuquerque, Krasna, & McLaughlin) 1992;54:980–2,CR
- Hypothermic thoracic and thoracoabdominal aneurysm operation: a central cannulation technique (Westaby) 1992;54:253–8*
- Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation (Tsuchida, Hashimoto, & others) 1992;54:161–3,CR
- Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms (Yamashita, Nakamura, & others) 1992;54:566–8,CR
- Surgical reconstruction of an ascending aortic dissection in Takayasu's arteritis (Haga, Yoshizu, & others) 1992;54:359–60,CR
- Technique of open distal anastomosis for repair of descending thoracic aortic aneurysms (Cooley & Baldwin) 1992;54:932–6*
- Thoracic aortic operations in patients aged 70 years or older (Tabayashi, Ohmi, & others) 1992;54:279–82*

Aortic coarctation
- Balloon angioplasty in the treatment of aortic coarctation (Ergina & Tchervenkov) 1992;54:599–600,CP; Reply (Rao & Chopra) 1992;54:600–2,CP
- Coarctation of the aorta in infants: does the aortic arch grow after repair? (Myers, McConnell, & Waldhausen) 1992;54:869–75*
- Coarctation repair in neonates with subclavian-sparing advancement flap (Sharma, Calderon, & Ott) 1992;54:137–41*

Aortic diseases
- Aortoesophageal fistula induced by foreign bodies (Wu & Lai) 1992;54:155–6,CR

Aortic valve
- Aortic valve repair (Cosgrove) 1992;54:1014–5,KR
- Approach for insertion of aortic composite valve grafts (Svensson) 1992;54:376–8,HW
- Combined traumatic avulsion of the aortic valve and rupture of the left common carotid artery (van Heurn, Hamerlijnck, & others) 1992;54:157–8,CR
- Magnetic resonance imaging evaluation of recipient for cryopreserved aortic allograft (Kon, Link, & others) 1992;54:39–43*
- Ross' first homograft replacement of the aortic valve (Gunning) 1992;54:809,CP; Reply (Hopkins) 1992;54:809–10,CP; Reply (Ross) 1992;54:810,CP
- Safety and efficacy of autologous blood donation before elective aortic valve operation (Dzik, Fleisher, & others) 1992;54:1177–81*
- Stentless porcine and pericardial valve in aortic position (Casabona, De Paulis, & others) 1992;54:681–5*

Aortic valve insufficiency
- Homograft root replacement for juvenile rheumatoid aortic valve incompetence (Schoof, van Suylen, & Bos) 1992;54:602,CP; Reply (Keeley) 1992;54:602–3,CP

Aortic valve stenosis
- Combined conventional mechanical and ultrasonic debridement for aortic valvular stenosis (Baeza, Majid, & others) 1992;54:62–7*
- Congenital aortic stenosis and patent ductus arteriosus in the adult (Glower, Bashore, & Spritzer) 1992;54:368–70,CR
- Optimum treatment of discrete subaortic stenosis (Lupinetti, Pridjian, & others) 1992;54:467–71*
- Surgical management of left coronary artery ostial atresia and supravalvar aortic stenosis (Rosenkranz, Murphy, & Cosgrove) 1992;54:779–81,CR
- Surgical treatment of postinfarction ventricular septal defect with aortic stenosis (Boglioli, Traill, & others) 1992;54:1209–11,CR
- Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*

Aortopulmonary window
- New surgical technique for total-defect aortopulmonary window (Matsuki, Yagihara, & others) 1992;54:991–2,HW

Aprotinin
- Aprotinin therapy for reoperative myocardial revascularization: a placebo-controlled study (Cosgrove, Heric, & others) 1992;54:1031–8*
- Aprotinin treatment during open heart operation in a patient with severe thrombocytopenia (Deviri, Izhar, & others) 1992;54:1018–9,CP
- Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin (Lamarra, Azzu, & Kulatilake) 1992;54:361–3,CR
- High-dose aprotinin in emergency coronary artery bypass after thrombolysis (Alajmo & Calamai) 1992;54:1022,CP; Reply (Efstratiadis, Munsch, & others) 1992;54:1022–3,CP
- Low-dose aprotinin in internal mammary artery bypass operations contributes to important blood saving (Schönberger, Everts, & others) 1992;54:1172–6*

Arrhythmia
- Electrophysiologic study of dysrhythmias after atrial operations in dogs (Tamiya, Yamashiro, & others) 1992;54:717–24*

Arteries
- Right internal mammary artery extended with an inferior epigastric artery for circumflex and right coronary bypass (Buche, Schroeder, & others) 1992;54:381–3,HW

Arteriovenous fistula
- Aneurysm of coronary arteriovenous fistula presenting as a calcified mediastinal mass (Okita, Miki, & others) 1992;54:771–3,CR

Aspergilloma
- Pleuropulmonary aspergilloma: clinical spectrum and results of surgical treatment (Massard, Roeslin, & others) 1992;54:1159–64*

Atelectasis
Pulmonary pseudotumor (Fadhli) 1992;54:1246,CP
Atherectomy
Post-atherectomy coronary artery aneurysm (Cohen, Banks, & others) 1992;54:1216–8,CR
Atrial fibrillation
Combined maze procedure and septal myectomy in a septuagenarian (Blitz, McLoughlin, & others) 1992;54:364–5,CR
Left atrial isolation associated with mitral valve operations (Graffigna, Pagani, & others) 1992;54:1093–8*

Banding
A staged expanding pulmonary artery band (Warren, Heath, & Brand) 1992;54:240–3*
Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*
Barbiturates
Barbiturates impair cerebral metabolism during hypothermic circulatory arrest (Siegman, Anderson, & others) 1992;54:1131–6*
Barrett's esophagus
Barrett's esophagus with high-grade dysplasia: an indication for esophagectomy? (Pera, Trastek, & others) 1992;54:199–204*
Current concepts concerning the nature and treatment of Barrett's esophagus and its complications (Streitz, Williamson, & Ellis) 1992;54:586–91,CV
Bioprosthesis
Early structural deterioration with the Mitroflow pericardial xenograft in the mitral position (Bernal, Rabasa, & others) 1992;54:152–4,CR
The Meadox-Gabbay pericardial xenograft: failure of the unicusp principle (Bortolotti, Ius, & others) 1992;54:952–8*
Biopsy
Open lung biopsy for diffuse infiltrative lung disease (Chechani, Landreneau, & Shaikh) 1992;54:296–300*
Role of open lung biopsy in diagnosing pulmonary complications of AIDS (Trachiotis, Hafner, & others) 1992;54:898–902*
Thoracoscopic lung biopsy (McKeown, Conant, & Hubbell) 1992;54:490–2*
Blastomycosis
Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis (Lagerstrom, Mitchell, & others) 1992;54:764–5,CR
Blood circulation
Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR
Cerebral blood flow and metabolism in hypothermic circulatory arrest (Mezrow, Sadeghi, & others) 1992;54:609–16*
Competitive flow from a fully patent coronary artery does not limit acute mammary graft flow (Spence, Lust, & others) 1992;54:21–6*
Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping (Svensson, Crawford, & others) 1992;54:74–9*
Blood coagulation disorders
Coagulation defects in neonates during cardiopulmonary bypass (Kern, Morana, & others) 1992;54:541–6*
Blood transfusion
Plateletpheresis and transfusion practice in heart operations (Davies, Wells, & others) 1992;54:1020,CP
Rapid transfusion after aortic decannulation (Bernal, Rabasa, & Revuelta) 1992;54:816,CP
Blood transfusion, autologous
Safety and efficacy of autologous blood donation before elective aortic valve operation (Dzik, Fleisher, & others) 1992;54:1177–81*
Subcutaneous use of erythropoietin in heart surgery (Watanabe, Fuse, & others) 1992;54:479–84*
Blood vessels
Vascular anatomy of the gastric tube used for esophageal reconstruction (Liebermann-Meffert, Meier, & Siewert) 1992;54:1110–5*
Body temperature
Temperature monitoring during CPB in infants: does it predict efficient brain cooling? (Kern, Jonas, & others) 1992;54:749–54*
Book reviews
Cardiac and Noncardiac Complications of Open Heart Surgery: Prevention, Diagnosis and Treatment, edited by Kotler & Alfieri (Nielsen) 1992;54:1015,RV
Mediastinal surgery, edited by Shields (Nielsen) 1992;54:781,RV
A Textbook of Cardioplegia for Difficult Clinical Problems, edited by Engelman & Levitsky (Sako) 1992;54:994,RV
Brain
Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest (Anderson, Siegman, & others) 1992;54:1126–30*
Temperature monitoring during CPB in infants: does it predict efficient brain cooling? (Kern, Jonas, & others) 1992;54:749–54*
Brain diseases, metabolic
Barbiturates impair cerebral metabolism during hypothermic circulatory arrest (Siegman, Anderson, & others) 1992;54:1131–6*
Brain injuries
Cerebral blood flow and metabolism in hypothermic circulatory arrest (Mezrow, Sadeghi, & others) 1992;54:609–16*
Breast neoplasms
Long-term survival after resection of pulmonary metastases from carcinoma of the breast (Lanza, Natarajan, & others) 1992;54:244–8*
Bronchi
Double-lung transplantation using donor lungs with a right tracheal bronchus (Brichon, Blin, & others) 1992;54:777–8,CR
Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Rickets) 1992;54:177–83,CT
Bronchial arteries
Role of the bronchial arteries in lung function (Ventemiglia) 1992;54:395–6,CP; Reply (Schreinemakers, De Leyn, & others) 1992;54:396–7,CP; Reply (Couraud, Baudet, & others) 1992;54:397,CP
Bronchial diseases
Expanding wire stents in benign tracheobronchial disease: indications and complications (Nashef, Dromer, & others) 1992;54:937–40*
Management of severe bronchial ischemia after bilateral sequential lung transplantation (Oturanlar, Klepetko, & others) 1992;54:1221–2,CR
Bronchial fistula
Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP

Bronchial fistula (cont'd)
  Treatment of AIDS-related bronchopleural fistula by pleurectomy (Crawford, Galloway, & others) 1992;54:212–5*
Bronchial neoplasms
  Bronchial carcinoid tumors: a retrospective analysis of 126 patients (Harpole, Feldman, & others) 1992;54:50–5*
  Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy (Tedder, Anstadt, & others) 1992;54:387–91,CV
  Effect of light dose on the photodynamic destruction of endobronchial tumors (McCaughan, Hawley, & others) 1992; 54:705–11*
Bronchoscopy
  Role of open lung biopsy in diagnosing pulmonary complications of AIDS (Trachiotis, Hafner, & others) 1992;54:898–902*

Carbon dioxide
  Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR
Carcinoid tumor
  Bronchial carcinoid tumors: a retrospective analysis of 126 patients (Harpole, Feldman, & others) 1992;54:50–5*
Carcinoma, bronchogenic
  Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy (Tedder, Anstadt, & others) 1992;54:387–91,CV
Carcinoma, non–small cell lung
  Better salvage in non–small cell lung cancer (Chambers) 1992; 54:399–400,CP
  Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*
  Radical laser segmentectomy for T1 N0 lung cancer (Kodama, Doi, & others) 1992;54:1193–5*
  Surgical treatment for higher stage non–small cell lung cancer (Van Raemdonck, Schneider, & Ginsberg) 1992;54:999–1013,CV
  Survival after resection of stage II non–small cell lung cancer (Martini, Burt, & others) 1992;54:460–6*
Carcinoma, oat cell
  Multimodal therapy of small cell lung cancer in TNM stages I through IIIa (Müller, Salzer, & others) 1992;54:493–7*
  Results of operation without adjuvant therapy in the treatment of small cell lung cancer (Shah, Thompson, & Goldstraw) 1992;54:498–501*
Carcinoma, renal cell
  Renal cell carcinoma: resection of solitary and multiple metastases (Pogrebniak, Haas, & others) 1992;54:33–8*
Cardiac nerves
  Human cardiac nerve stimulation (Murphy & Armour) 1992; 54:502–6*
Cardiac output
  Comparison of cardiac output measured by intrapulmonary artery Doppler, thermodilution, and electromagnetometry (Heerdt, Pond, & others) 1992;54:959–66*
Cardiac pacing, artificial
  Atrioventricular pacing in congenital heart disease (Kratz, Gillette, & others) 1992;54:485–9*
  Unusual complication of temporary pacing wires in children (Bolton & Mayer) 1992;54:769–70,CR
Cardiac tamponade
  Usefulness of right ventricular indices in early diagnosis of cardiac tamponade (Jones, Izzat, & others) 1992;54:44–9*
Cardiomyopathy, hypertrophic
  Combined maze procedure and septal myectomy in a septuagenarian (Blitz, McLoughlin, & others) 1992;54:364–5,CR
Cardiomyoplasty
  Clinical cardiomyoplasty: preoperative factors associated with outcome (Furnary, Magovern, & others) 1992;54:1139–43*
  Dynamic cardiomyoplasty (Chiu) 1992;54:592–3,KR
Cardioplegic solutions
  Myocardial protection of neonatal heart by cardioplegic solution with recombinant human superoxide dismutase (Tatebe, Nakazawa, & others) 1992;54:124–9*
  Vascular and interstitial effect of University of Wisconsin solution on canine lung (Unruh) 1992;54:1168–71*
Cardiopulmonary bypass
  Benefits of combined balloon pumping and percutaneous cardiopulmonary bypass (Phillips, Zeff, & others) 1992;54: 908–10*
  Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin (Lamarra, Azzu, & Kulatilake) 1992;54:361–3,CR
  Chronic, traumatic pseudoaneurysm of the ascending aorta (Albuquerque, Krasna, & McLaughlin) 1992;54:980–2,CR
  Coagulation defects in neonates during cardiopulmonary bypass (Kern, Morana, & others) 1992;54:541–6*
  Concomitant cardiac and pulmonary operation: the role of cardiopulmonary bypass (Ulicny, Schmelzer, & others) 1992;54:289–95*
  Coronary artery bypass without cardiopulmonary bypass (Pfister, Zaki, & others) 1992;54:1085–92*
  Emergent applications of cardiopulmonary support: a multi-institutional experience (Hill, Bruhn, & others) 1992;54: 699–704*
  Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass (Jansen, van Oeveren, & others) 1992;54:744–8*
  Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*
  Quantitation of particulate microemboli during cardiopulmonary bypass: experimental and clinical studies (Liu, Su, & Ding) 1992;54:1196–202*
  A randomized study of the systemic effects of warm heart surgery (Christakis, Koch, & others) 1992;54:449–59*
  Rapid transfusion after aortic decannulation (Bernal, Rabasa, & Revuelta) 1992;54:816,CP
  Release of vasoactive substances during cardiopulmonary bypass (Downing & Edmunds) 1992;54:1236–43,CV
  Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Ricketts) 1992;54:177–83,CT
  Temperature monitoring during CPB in infants: does it predict efficient brain cooling? (Kern, Jonas, & others) 1992;54: 749–54*
  Time for new concepts about measurement of complement activation by cardiopulmonary bypass? (Videm, Fosse, & others) 1992;54:725–31*
Carotid artery diseases
  Combined carotid and coronary revascularization: the preferred approach to the severe vasculopath (Rizzo, Whittemore, & others) 1992;54:1099–109*
  Combined traumatic avulsion of the aortic valve and rupture of the left common carotid artery (van Heurn, Hamerlijnck, & others) 1992;54:157–8,CR

Case reports
Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty (Bégin & Sheiner) 1992;54:564–5,CR
Aneurysm of coronary arteriovenous fistula presenting as a calcified mediastinal mass (Okita, Miki, & others) 1992;54:771–3,CR
Aneurysm of the ascending aorta after cardiac transplantation (Defraigne, Vahdat, & others) 1992;54:983–4,CR
Aortoesophageal fistula induced by foreign bodies (Wu & Lai) 1992;54:155–6,CR
Bilateral adrenal hemorrhage after an open heart operation (Ting, Nosher, & others) 1992;54:357–8,CR
Bilateral elastofibroma dorsi (Machens, Mechtersheimer, & others) 1992;54:774–6,CR
Bronchoenteric fistula from an infected internal cardioverter defibrillator (Birnbaum, Lichtenstein, & others) 1992;54:987–8,CR
Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR
Cardiac valve replacement in patients infected with the human immunodeficiency virus (Bräu, Esposito, & Simberkoff) 1992;54:552–4,CR
Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin (Lamarra, Azzu, & Kulatilake) 1992;54:361–3,CR
Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR
Chronic, traumatic pseudoaneurysm of the ascending aorta (Albuquerque, Krasna, & McLaughlin) 1992;54:980–2,CR
Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis (Lagerstrom, Mitchell, & others) 1992;54:764–5,CR
Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR
Combined maze procedure and septal myectomy in a septuagenarian (Blitz, McLoughlin, & others) 1992;54:364–5,CR
Combined traumatic avulsion of the aortic valve and rupture of the left common carotid artery (van Heurn, Hamerlijnck, & others) 1992;54:157–8,CR
Complete cure after a seemingly unsuccessful operation for Wolff-Parkinson-White syndrome (Rakovec, Brecelj, & Zupan) 1992;54:1203–5,CR
Congenital aortic stenosis and patent ductus arteriosus in the adult (Glower, Bashore, & Spritzer) 1992;54:368–70,CR
Coronary artery bypass grafting nine years after cardiac transplantation (Dunning, Kendall, & others) 1992;54:571–2,CR
Double-lung transplantation using donor lungs with a right tracheal bronchus (Brichon, Blin, & others) 1992;54:777–8,CR
Early structural deterioration with the Mitroflow pericardial xenograft in the mitral position (Bernal, Rabasa, & others) 1992;54:152–4,CR
Extracardiac total cavopulmonary connection (Laschinger, Ringel, & others) 1992;54:371–3,CR
Giant intrapericardial solitary fibrous tumor (Bortolotti, Calabrò, & others) 1992;54:1219–20,CR
Hyperbaric oxygen: value in management of nonhealing saphenectomy wounds (Horowitz, Portogues, & others) 1992;54:782–3,CR
Intercostal hemangioma presenting as a chest wall tumor (Winchester, Victor, & Fry) 1992;54:145–6,CR
Intraoperative echocardiographic diagnosis of previously unrecognized cor triatriatum (Hogue, Barzilai, & others) 1992;54:562–3,CR
Left ventricular diverticulum with hypertrophy of the left ventricular apex (Yamashita, Nakamura, & others) 1992;54:761–3,CR
Management of severe bronchial ischemia after bilateral sequential lung transplantation (Oturanlar, Klepetko, & others) 1992;54:1221–2,CR
Mediastinal window: a cause of simultaneous bilateral spontaneous pneumothorax (Juvonen, Lepojärvi, & others) 1992;54:560–1,CR
Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR
Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation (Tsuchida, Hashimoto, & others) 1992;54:161–3,CR
Pericardial repair of a tracheal laceration during transhiatal esophagectomy (Gorenstein, Abel, & Patterson) 1992;54:784–6,CR
Pericardioperitoneal shunt for persistent pericardial effusions: a new drainage procedure (Molnar & Jeyasingham) 1992;54:569–70,CR
Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia (Carroll, Kramer, & others) 1992;54:1212–3,CR
Pneumatocele complicating hyperimmunoglobulin E syndrome (Job's syndrome) (Shamberger, Wohl, & others) 1992;54:1206–8,CR
Post-atherectomy coronary artery aneurysm (Cohen, Banks, & others) 1992;54:1216–8,CR
Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy (Ziemer, Heinemann, & others) 1992;54:971–3,CR
Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR
Replacement of the valvular prosthesis in a patient with a Bentall procedure (Panos, Teoh, & others) 1992;54:555–6,CR
Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms (Yamashita, Nakamura, & others) 1992;54:566–8,CR
Retrograde coronary sinus cardioplegia in the presence of persistent left superior vena cava (Shahian) 1992;54:1214–5,CR
Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis (Smith & Goldstein) 1992;54:766–8,CR
Simplified correction of outflow obstruction after mitral valve replacement (Reed & Iverson) 1992;54:985–6,CR
Surgical management of left coronary artery ostial atresia and supravalvar aortic stenosis (Rosenkranz, Murphy, & Cosgrove) 1992;54:779–81,CR
Surgical reconstruction of an ascending aortic dissection in Takayasu's arteritis (Haga, Yoshizu, & others) 1992;54:359–60,CR
Surgical treatment of postinfarction ventricular septal defect with aortic stenosis (Boglioli, Traill, & others) 1992;54:1209–11,CR
Surgically created Wolff-Parkinson-White syndrome after Fontan operation (Razzouk, Gow, & others) 1992;54:974–7,CR
Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries (Yoshimura, Yamaguchi, & others) 1992;54:573–5,CR

Case reports (cont'd)
- Thoracoscopic resection of an anterior mediastinal tumor (Landreneau, Dowling, & others) 1992;54:142–4,CR
- Total correction of transposition of great arteries with atrioventricular septal defect (Kumar, Prabhakar, & others) 1992; 54:989–90,CR
- Tracheoesophageal fistula after chemotherapy for lymphoma (Sharpe, Sendegeya, & others) 1992;54:366–7,CR
- Tricuspid valve obstruction caused by plasmacytoma metastasis (Carrel, Linka, & Turina) 1992;54:352–4,CR
- True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient (Baldwin, Klima, & others) 1992;54:978–9,CR
- Unusual complication of temporary pacing wires in children (Bolton & Mayer) 1992;54:769–70,CR

Catheterization
- Directed atraumatic coronary sinus cannulation for retrograde cardioplegia administration (Aldea, Connelly, & others) 1992;54:789–90,HW
- Hypothermic thoracic and thoracoabdominal aneurysm operation: a central cannulation technique (Westaby) 1992;54: 253–8*
- Management of aortic cannulation site blowouts (Szentpetery) 1992;54:582–3,HW
- Newly developed holder for a right-angled metal venous cannula (Watanabe, Abe, & others) 1992;54:993–4,HW
- Rapid transfusion after aortic decannulation (Bernal, Rabasa, & Revuelta) 1992;54:816,CP
- Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW

Cavopulmonary connection
- Extracardiac total cavopulmonary connection (Laschinger, Ringel, & others) 1992;54:371–3,CR

Cerebral ischemia
- Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery (Menasché, Fleury, & Piwnica) 1992;54:392–3,UP
- Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest (Anderson, Siegman, & others) 1992;54: 1126–30*

Cerebrum
- Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms (Yamashita, Nakamura, & others) 1992;54: 566–8,CR

Chemotherapy
- Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results (Parker) 1992;54:808,UP

Child
- Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation (Vouhé, Tamisier, & others) 1992;54:621–7*
- Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR
- Extracardiac total cavopulmonary connection (Laschinger, Ringel, & others) 1992;54:371–3,CR
- Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation (Ziomek, Harrell, & others) 1992;54:861–8*
- Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis (Leung, Lee, & others) 1992;54:523–7*
- Partial median sternotomy for repair of heart defects: a cosmetic approach (Wilson, Ilbawi, & others) 1992;54:892–3*
- Pediatric lung transplantation for pulmonary hypertension and congenital heart disease (Spray, Mallory, & others) 1992; 54:216–25*
- Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR
- Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW
- Surgical management of infective endocarditis in children (Citak, Rees, & Mavroudis) 1992;54:755–60*
- Surgical management of left coronary artery ostial atresia and supravalvar aortic stenosis (Rosenkranz, Murphy, & Cosgrove) 1992;54:779–81,CR
- Unusual complication of temporary pacing wires in children (Bolton & Mayer) 1992;54:769–70,CR

Chondrosarcoma
- Primary bony and cartilaginous sarcomas of chest wall: results of therapy (Burt, Fulton, & others) 1992;54:226–32*

Chylothorax
- Successful treatment of postoperative chylothorax using an external pleuroperitoneal shunt (Cummings, Wyatt, & others) 1992;54:276–8*

Cineangiography
- Surgical considerations in bypassing coronary arteries with 100% proximal occlusion (McLean, Svensson, & others) 1992;54:894–7*

Clagett procedure
- Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR

Classics in thoracic surgery
- Clarence Crafoord and the first successful resection of a cardiac myxoma (Chitwood) 1992;54:997–8,CL
- The Nissen fundoplication (Ellis) 1992;54:1231–5,CL

Collective review
- Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Ricketts) 1992;54:177–83,CT

Commissurotomy
- Acute pulmonary edema in closed mitral commissurotomy (Tewari & Kumar) 1992;54:191,CP

Complement activation
- Time for new concepts about measurement of complement activation by cardiopulmonary bypass? (Videm, Fosse, & others) 1992;54:725–31*

Computer systems
- Team approach for clinical cardiac surgery research (Canver & Fiedler) 1992;54:1244,CP

Cor triatriatum
- Intraoperative echocardiographic diagnosis of previously unrecognized cor triatriatum (Hogue, Barzilai, & others) 1992;54:562–3,CR

Coronary aneurysm
- Aneurysm of coronary arteriovenous fistula presenting as a calcified mediastinal mass (Okita, Miki, & others) 1992;54: 771–3,CR
- Does a posterior aneurysm increase the risk of endocardial resection? (Kron, Kern, & others) 1992;54:617–20*
- Post-atherectomy coronary artery aneurysm (Cohen, Banks, & others) 1992;54:1216–8,CR

Coronary artery bypass
- Allogenic vein as a conduit for coronary artery bypass (Barner) 1992;54:817,ED

  - Bioassay of EDRF from internal mammary arteries: implications for early and late bypass patency (Pearson, Evora, & Schaff) 1992;54:1078–84*
  - Combined carotid and coronary revascularization: the preferred approach to the severe vasculopath (Rizzo, Whittemore, & others) 1992;54:1099–109*
  - Competitive flow from a fully patent coronary artery does not limit acute mammary graft flow (Spence, Lust, & others) 1992;54:21–6*
  - Coronary artery bypass grafting nine years after cardiac transplantation (Dunning, Kendall, & others) 1992;54:571–2,CR
  - Coronary artery bypass using internal mammary artery branches (Morin, Hedderich, & others) 1992;54:911–4*
  - Coronary artery bypass without cardiopulmonary bypass (Pfister, Zaki, & others) 1992;54:1085–92*
  - Coronary bypass graft aneurysm (Dimitri & Reid) 1992:54; 395,CP
  - Cryopreserved allograft veins as alternative coronary artery bypass conduits: early phase results (Laub, Muralidharan, & others) 1992;54:826–31*
  - High-dose aprotinin in emergency coronary artery bypass after thrombolysis (Alajmo & Calamai) 1992;54:1022,CP; Reply (Efstratiadis, Munsch, & others) 1992;54:1022–3,CP
  - Ischemic mitral valve repair (Cheng) 1992;54:190–1,CP
  - Length of the in situ right gastroepiploic artery for coronary artery bypass (Tavilla) 1992;54:1244–5,CP; Reply (Suma) 1992;54:1245,CP
  - Postinfarct ventricular septal defect repair: effect of coronary artery bypass grafting (Muehrcke, Daggett, & others) 1992;54:876–83*
  - Revival of the radial artery for coronary artery bypass grafting (Acar, Jebara, & others) 1992;54:652–60*
  - Right internal mammary artery extended with an inferior epigastric artery for circumflex and right coronary bypass (Buche, Schroeder, & others) 1992;54:381–3,HW
  - Risk analysis of operative intervention for failed coronary angioplasty (Borkon, Failing, & others) 1992;54:884–91*
  - Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis (Smith & Goldstein) 1992;54:766–8,CR
  - Surgical considerations in bypassing coronary arteries with 100% proximal occlusion (McLean, Svensson, & others) 1992;54:894–7*
  - True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient (Baldwin, Klima, & others) 1992;54:978–9,CR
- **Coronary disease**
  - Acute severe postischemic myocardial depression reversed by triiodothyronine (Holland, Brown, & Clark) 1992;54:301–5*
  - Congenital malformations of the coronary arteries: the Texas Heart Institute experience (Fernandes, Kadivar, & others) 1992;54:732–40*
  - Heterotopic heart transplantation and recipient heart operation in ischemic heart disease (Ridley, Khaghani, & others) 1992;54:333–7*
  - Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*
  - Surgical considerations in bypassing coronary arteries with 100% proximal occlusion (McLean, Svensson, & others) 1992;54:894–7*
  - Surgical management of left coronary artery ostial atresia and supravalvar aortic stenosis (Rosenkranz, Murphy, & Cosgrove) 1992;54:779–81,CR
- **Coronary vessels**
  - Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation (Vouhé, Tamisier, & others) 1992;54:621–7*
  - Coronary sinus injuries during retrograde continuous normothermic blood cardioplegia (Panos, Ali, & others) 1992;54: 1137–8*
- **Correction**
  - "Thoracic spine fractures and aortic rupture: a significant and fatal association" (Sturm, Hynes, & Perry) 1992;54:603,CP
- **Correspondence**
  - Abrupt cardiac failure using a right VAD in the presence of a tricuspid valve prosthesis (Griffin & Dark) 1992;54:1023–4,CP
  - Acute pulmonary edema in closed mitral commissurotomy (Tewari & Kumar) 1992;54:191,CP
  - Aprotinin treatment during open heart operation in a patient with severe thrombocytopenia (Deviri, Izhar, & others) 1992;54:1018–9,CP
  - Balloon angioplasty in the treatment of aortic coarctation (Ergina & Tchervenkov) 1992;54:599–600,CP; Reply (Rao & Chopra) 1992;54:600–2,CP
  - Better salvage in non-small cell lung cancer (Chambers) 1992; 54:399–400,CP
  - The blue man phenomenon (Mitchell, Saunders, & others) 1992;54:814,CP
  - Bronchial stump closure (Hoffman & Frater) 1992;54:399,CP
  - Continuous normothermic blood cardioplegia: simplified delivery circuit (Satyanarayana, Rao, & others) 1992;54: 810,CP
  - Coronary bypass graft aneurysm (Dimitri & Reid) 1992:54; 395,CP
  - Electrical instability during reperfusion (Holman) 1992;54: 1245–6,CP
  - Esophageal perforation (Attar) 1992;54:809,CP; Reply (Jones & Ginsberg) 1992;54:809,CP
  - Extended approach to the mitral valve (Sampathkumar) 1992; 54:596–7,CP; Reply (Guiraudon) 1992;54:597–8,CP
  - Hemodynamic effects of pericardial closure (Sampathkumar) 1992;54:1023,CP; Reply (Hunter & Angelini) 1992;54: 1023,CP
  - Hemolysis after open heart operations (Golino, Stassano, & Spampinato) 1992;54:1246–7,CP; Reply (Okita & Miki) 1992;54:1247,CP
  - High-dose aprotinin in emergency coronary artery bypass after thrombolysis (Alajmo & Calamai) 1992;54:1022,CP; Reply (Efstratiadis, Munsch, & others) 1992;54:1022–3,CP
  - Homograft root replacement for juvenile rheumatoid aortic valve incompetence (Schoof, van Suylen, & Bos) 1992;54: 602,CP; Reply (Keeley) 1992;54:602–3,CP
  - Internal mammary artery to lung parenchyma fistula (Wood) 1992;54:603,CP; Reply (Blanche) 1992;54:603,CP
  - Ischemic mitral valve repair (Cheng) 1992;54:190–1,CP
  - Length of the in situ right gastroepiploic artery for coronary artery bypass (Tavilla) 1992;54:1244–5,CP; Reply (Suma) 1992;54:1245,CP
  - Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
  - Minimal hemodilution and optimal potassium use during normothermic aerobic arrest (Le Houerou, Singh, & others) 1992;54:815–6,CP
  - Modified retractor to prevent peripheral nerve injury (Ancalmo) 1992;54:1249,CP
  - Modified technique of internal mammary artery harvest (Sirivella, Gielchinsky, & Parsonnet) 1992;54:190,CP; Reply (John, Edmondson, & Rees) 1992;54:190,CP
  - A new idea (Neptune) 1992;54:188,CP

Correspondence (cont'd)
Palliative intubation for dysphagia (Wetstein) 1992;54:813–4,CP; Reply (Liakakos, Ohri, & others) 1992;54:814,CP
Penetrating cardiac trauma (Ivatury & Rohman) 1992;54:1247–8,CP; Reply (Knott-Craig) 1992;54:1248,CP
Pericardial window (Weissberg) 1992;54:191–2,CP; Reply (Attar & McLaughlin) 1992;54:192,CP; Reply (Spodick) 1992;54:192,CP
Plateletpheresis and transfusion practice in heart operations (Davies, Wells, & others) 1992;54:1020,CP
Preoperative morphologic and physiologic assessment of internal thoracic arteries (Canver) 1992;54:1020–1,CP; Reply (Grover) 1992;54:1021,CP
Profound hypothermia and circulatory arrest (Baudet) 1992;54:596,CP; Reply (Rainer) 1992;54:596,CP
Pulmonary pseudotumor (Fadhli) 1992;54:1246,CP
Rapid transfusion after aortic decannulation (Bernal, Rabasa, & Revuelta) 1992;54:816,CP
Rereplacement of the mitral valve with represervation of the subvalvular apparatus (Olinger) 1992;54:188–90,CP
Retrograde disc escape in a Harken mitral valve prosthesis (Berger) 1992;54:394,CP; Reply (Otero-Coto) 1992:54;394–5,CP
Role of the bronchial arteries in lung function (Ventemiglia) 1992;54:395–6,CP; Reply (Schreinemakers, De Leyn, & others) 1992;54:396–7,CP; Reply (Couraud, Baudet, & others) 1992;54:397,CP
Ross' first homograft replacement of the aortic valve (Gunning) 1992;54:809,CP; Reply (Hopkins) 1992;54:809–10,CP; Reply (Ross) 1992;54:810,CP
Surgery of aortic dissections with GRF glue (Zeplin) 1992;54:1248–9,CP
Surgical management of carcinoid heart disease (Aldrete) 1992;54:598,CP; Reply (Davis) 1992;54:598,CP
Surgical stabilization of the flail chest (Borioni, Ciani, & others) 1992;54:397–8,CP; Reply (Landreneau) 1992;54:398,CP
Team approach for clinical cardiac surgery research (Canver & Fiedler) 1992;54:1244,CP
Thermo Cardiosystems left ventricular assist device (Frazier) 1992;54:1019,CP; Reply (Burton, Phillips, & others) 1992;54:1019–20,CP
Thromboelastogram and postoperative hemorrhage (Spiess) 1992;54:810–1,CP (Tuman, McCarthy, & Ivankovich) 1992;54:811–2,CP; (Martin, Horkay, & others) 1992;54:812–3,CP; Reply (Lin & Wang) 1992;54:813,CP
Total orthotopic heart transplantation: an alternative to the standard technique (Kendall, Ciulli, & others) 1992;54:187,CP; Reply (Dreyfus) 1992;54:187–8,CP
Visualization of coronary artery anastomoses by gas jet (Poulton) 1992;54:598–9,CP; Reply (Salerno & Teoh) 1992;54:599,CP
Counterpulsation
Intraaortic balloon counterpulsation: patterns of usage and outcome in cardiac surgery patients (Creswell, Rosenbloom, & others) 1992;54:11–20*
Cryopreservation
Magnetic resonance imaging evaluation of recipient for cryopreserved aortic allograft (Kon, Link, & others) 1992;54:39–43*
Current reviews
Current concepts concerning the nature and treatment of Barrett's esophagus and its complications (Streitz, Williamson, & Ellis) 1992;54:586–91,CV
Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy (Tedder, Anstadt, & others) 1992;54:387–91,CV
Release of vasoactive substances during cardiopulmonary bypass (Downing & Edmunds) 1992;54:1236–43,CV
Surgical treatment for higher stage non–small cell lung cancer (Van Raemdonck, Schneider, & Ginsberg) 1992;54:999–1013,CV
Video-assisted thoracic surgery: basic technical concepts and intercostal approach strategies (Landreneau, Mack, & others) 1992;54:800–7,CV
Cyanosis
Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR
Cyclosporins
Use of epicardial electrocardiograms for detecting cardiac allograft rejection (Irwin, Binco, & others) 1992;54:669–75*
Cystic fibrosis
Double-lung transplantation for cystic fibrosis (Shennib, Noirclerc, & others) 1992;54:27–32*
Cysts
Pneumatocele complicating hyperimmunoglobulin E syndrome (Job's syndrome) (Shamberger, Wohl, & others) 1992;54:1206–8,CR

Debridement
Combined conventional mechanical and ultrasonic debridement for aortic valvular stenosis (Baeza, Majid, & others) 1992;54:62–7*
Decompression
Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW
Deglutition disorders
Palliative intubation for dysphagia (Wetstein) 1992;54:813–4,CP; Reply (Liakakos, Ohri, & others) 1992;54:814,CP
Dissection
Considerations in the skeletonization technique of internal thoracic artery dissection (Cunningham, Gharavi, & others) 1992;54:947–51*
Optimal approach to the mitral valve: dissection of the interatrial groove (Larbalestier, Chard, & Cohn) 1992;54:1186–8*
Surgery of aortic dissections with GRF glue (Zeplin) 1992;54:1248–9,CP
Diverticulum
Left ventricular diverticulum with hypertrophy of the left ventricular apex (Yamashita, Nakamura, & others) 1992;54:761–3,CR
Drainage
Modified urinary collecting bags for prolonged underwater chest drainage (Bar-El, Lieberman, & Yellin) 1992;54:995–6,HW
Drug toxicity
The blue man phenomenon (Mitchell, Saunders, & others) 1992;54:814,CP
Ductus arteriosus, patent
Congenital aortic stenosis and patent ductus arteriosus in the adult (Glower, Bashore, & Spritzer) 1992;54:368–70,CR
Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54:164–5,HW

Ebstein's anomaly

Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis (Leung, Lee, & others) 1992;54:523–7*

Echocardiography

Directed atraumatic coronary sinus cannulation for retrograde cardioplegia administration (Aldea, Connelly, & others) 1992;54:789–90,HW

Intraoperative echocardiographic diagnosis of previously unrecognized cor triatriatum (Hogue, Barzilai, & others) 1992;54:562–3,CR

Echocardiography, Doppler

Comparison of cardiac output measured by intrapulmonary artery Doppler, thermodilution, and electromagnetometry (Heerdt, Pond, & others) 1992;54:959–66*

The learning curve for intraoperative echocardiography during congenital heart surgery (Ungerleider, Greeley, & others) 1992;54:691–8*

Editorials

Allogenic vein as a conduit for coronary artery bypass (Barner) 1992;54:817,ED

Heterotopic transplantation: is it a viable alternative? (Baumgartner) 1992;54:401–2,ED

Lobectomy without a rib spreader (McKneally) 1992;54:2,ED

Electric countershock

Bilateral anterior thoracotomy for automatic implantable cardioverter defibrillator placement in patients with previous sternotomy (Karwande & Rowles) 1992;54:791–3,HW

Bronchoenteric fistula from an infected internal cardioverter defibrillator (Birnbaum, Lichtenstein, & others) 1992;54:987–8,CR

Subfascial implantation of implantable cardioverter defibrillator generator (Shahian, Williamson, & others) 1992;54:173–4,HW

Electrocardiography

Use of epicardial electrocardiograms for detecting cardiac allograft rejection (Irwin, Binco, & others) 1992;54:669–75*

Electrodes

Comparison of 180-degree and 360-degree skeletal muscle nerve cuff electrodes (Letsou, Hogan, & others) 1992;54:925–31*

Electromagnetics

Comparison of cardiac output measured by intrapulmonary artery Doppler, thermodilution, and electromagnetometry (Heerdt, Pond, & others) 1992;54:959–66*

Electrophysiology

Comparison of 180-degree and 360-degree skeletal muscle nerve cuff electrodes (Letsou, Hogan, & others) 1992;54:925–31*

Electrophysiologic study of dysrhythmias after atrial operations in dogs (Tamiya, Yamashiro, & others) 1992;54:717–24*

Embolism

Quantitation of particulate microemboli during cardiopulmonary bypass: experimental and clinical studies (Liu, Su, & Ding) 1992;54:1196–202*

Embolism, air

Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery (Menasché, Fleury, & Piwnica) 1992;54:392–3,UP

Empyema

Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR

Endarterectomy

Combined carotid and coronary revascularization: the preferred approach to the severe vasculopath (Rizzo, Whittemore, & others) 1992;54:1099–109*

Endocarditis

Cardiac valve replacement in patients infected with the human immunodeficiency virus (Bräu, Esposito, & Simberkoff) 1992;54:552–4,CR

Surgical management of infective endocarditis in children (Citak, Rees, & Mavroudis) 1992;54:755–60*

Endocardium

Does a posterior aneurysm increase the risk of endocardial resection? (Kron, Kern, & others) 1992;54:617–20*

Endomyocardial fibrosis

Mitral valve repair in patients with endomyocardial fibrosis (Uva, Jebara, & others) 1992;54:89–92*

Endothelium-derived relaxing factor

Bioassay of EDRF from internal mammary arteries: implications for early and late bypass patency (Pearson, Evora, & Schaff) 1992;54:1078–84*

Endotoxins

Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass (Jansen, van Oeveren, & others) 1992;54:744–8*

Erythropoietin

Subcutaneous use of erythropoietin in heart surgery (Watanabe, Fuse, & others) 1992;54:479–84*

Esophageal diseases

Barrett's esophagus with high-grade dysplasia: an indication for esophagectomy? (Pera, Trastek, & others) 1992;54:199–204*

Esophageal fistula

Aortoesophageal fistula induced by foreign bodies (Wu & Lai) 1992;54:155–6,CR

Esophageal neoplasms

Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results (Parker) 1992;54:808,UP

Palliative intubation for dysphagia (Wetstein) 1992;54:813–4,CP; Reply (Liakakos, Ohri, & others) 1992;54:814,CP

Videothoracoscopic enucleation of esophageal leiomyoma (Bardini, Segalin, & others) 1992;54:576–7,HW

Esophageal perforation

Esophageal perforation (Attar) 1992;54:809,CP; Reply (Jones & Ginsberg) 1992;54:809,CP

Temporary double exclusion of the perforated esophagus using absorbable staples (Bardini, Bonavina, & others) 1992;54:1165–7*

Esophagectomy

Barrett's esophagus with high-grade dysplasia: an indication for esophagectomy? (Pera, Trastek, & others) 1992;54:199–204*

Pericardial repair of a tracheal laceration during transhiatal esophagectomy (Gorenstein, Abel, & Patterson) 1992;54:784–6,CR

Transhiatal esophagectomy: a safe alternative for selected patients (Daniel, Fleischer, & others) 1992;54:686–90*

Esophagocardiomyotomy

Long-term effect of total fundoplication on the myotomized esophagus (Topart, Deschamps, & others) 1992;54:1046–52*

Esophagogastrectomy

Esophagogastrectomy and the variant left hepatic artery (Hemming, Finley, & others) 1992;54:166–8,HW

Esophagogastrectomy (cont'd)
Vascular anatomy of the gastric tube used for esophageal reconstruction (Liebermann-Meffert, Meier, & Siewert) 1992;54:1110–5*
Esophagogastrostomy
Transoral cervical esophagogastrostomy using the EEA stapling device (Ancalmo) 1992;54:186,UP
Esophagus
Vascular anatomy of the gastric tube used for esophageal reconstruction (Liebermann-Meffert, Meier, & Siewert) 1992;54:1110–5*
Extracorporeal circulation
Predictive criteria for the need of extracorporeal circulation in single-lung transplantation (Hirt, Haverich, & others) 1992;54:676–80*
Extracorporeal membrane oxygenation
Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation (Ziomek, Harrell, & others) 1992;54:861–8*

Fee schedules
Physician payment reform: a bibliography (Miller) 1992;54:184–5,KR
Fenestra
Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR
Fibroma
Bilateral elastofibroma dorsi (Machens, Mechtersheimer, & others) 1992;54:774–6,CR
Fibrosis
Clinical manifestation of mediastinal fibrosis and histoplasmosis (Mathisen & Grillo) 1992;54:1053–8*
Fistula
Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty (Bégin & Sheiner) 1992;54:564–5,CR
Aortoesophageal fistula induced by foreign bodies (Wu & Lai) 1992;54:155–6,CR
Bronchoenteric fistula from an infected internal cardioverter defibrillator (Birnbaum, Lichtenstein, & others) 1992;54:987–8,CR
Internal mammary artery to lung parenchyma fistula (Wood) 1992;54:603,CP; Reply (Blanche) 1992;54:603,CP
Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
Treatment of AIDS-related bronchopleural fistula by pleurectomy (Crawford, Galloway, & others) 1992;54:212–5*
Fluorocarbons
Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery (Menasché, Fleury, & Piwnica) 1992;54:392–3,UP
Intrathecal perfusion of an oxygenated perfluorocarbon prevents paraplegia after aortic occlusion (Maughan, Mohan, & others) 1992;54:818–25*
Fluosol
Fluosol cardioplegia results in complete functional recovery: a comparison with blood cardioplegia (Pearl, Laks, & others) 1992;54:1144–50*
Foreign bodies
Aortoesophageal fistula induced by foreign bodies (Wu & Lai) 1992;54:155–6,CR
Free radicals
A prostacyclin analogue reduces free radical generation in heart-lung transplantation (Takeuchi, Suzuki, & others) 1992;54:327–32*
Fundoplication
Long-term effect of total fundoplication on the myotomized esophagus (Topart, Deschamps, & others) 1992;54:1046–52*
The Nissen fundoplication (Ellis) 1992;54:1231–5,CL

Gases
Visualization of coronary artery anastomoses by gas jet (Poulton) 1992;54:598–9,CP; Reply (Salerno & Teoh) 1992;54:599,CP
Gastric tube
Vascular anatomy of the gastric tube used for esophageal reconstruction (Liebermann-Meffert, Meier, & Siewert) 1992;54:1110–5*
Gastroepiploic artery
Length of the in situ right gastroepiploic artery for coronary artery bypass (Tavilla) 1992;54:1244–5,CP; Reply (Suma) 1992;54:1245,CP
Gastroesophageal reflux
Long-term effect of total fundoplication on the myotomized esophagus (Topart, Deschamps, & others) 1992;54:1046–52*
The Nissen fundoplication (Ellis) 1992;54:1231–5,CL
Geriatrics
Combined maze procedure and septal myectomy in a septuagenarian (Blitz, McLoughlin, & others) 1992;54:364–5,CR
Is use of the intraaortic balloon pump in octogenarians justified? (Sisto, Hoffman, & others) 1992;54:507–11*
Thoracic aortic operations in patients aged 70 years or older (Tabayashi, Ohmi, & others) 1992;54:279–82*
Glucose
Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*

Heart arrest, induced
Acadesine (AICA-riboside) improves postischemic cardiac recovery (Bolling, Groh, & others) 1992;54:93–8*
Continuous normothermic blood cardioplegia: simplified delivery circuit (Satyanarayana, Rao, & others) 1992;54:810,CP
Coronary sinus injuries during retrograde continuous normothermic blood cardioplegia (Panos, Ali, & others) 1992;54:1137–8*
Directed atraumatic coronary sinus cannulation for retrograde cardioplegia administration (Aldea, Connelly, & others) 1992;54:789–90,HW
Electrical instability during reperfusion (Holman) 1992;54:1245–6,CP
Fluosol cardioplegia results in complete functional recovery: a comparison with blood cardioplegia (Pearl, Laks, & others) 1992;54:1144–50*
Minimal hemodilution and optimal potassium use during normothermic aerobic arrest (Le Houerou, Singh, & others) 1992;54:815–6,CP
Nicardipine: myocardial protection in isolated working hearts (Mitchell, DeBoer, & others) 1992;54:712–6*
Normothermic cardioplegia: is aortic cross-clamping still synonymous with myocardial ischemia? (Menasché, Peynet, & others) 1992;54:472–8*
A randomized study of the systemic effects of warm heart surgery (Christakis, Koch, & others) 1992;54:449–59*
Retrograde coronary sinus cardioplegia in the presence of persistent left superior vena cava (Shahian) 1992;54:1214–5,CR

Retrograde versus antegrade cardioplegia: impact on right ventricular function (Douville, Kratz, & others) 1992;54:56–61*

Heart assist devices

Abrupt cardiac failure using a right VAD in the presence of a tricuspid valve prosthesis (Griffin & Dark) 1992;54:1023–4,CP

Device-supported myocardial revascularization: safe help for sick hearts (Sweeney & Frazier) 1992;54:1065–70*

Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW

Postcardiotomy centrifugal mechanical ventricular support (Golding, Crouch, & others) 1992;54:1059–64*

Replacement of paracorporeal ventricular assist devices (Lohmann, McBride, & others) 1992;54:1226–7,HW

Thermo Cardiosystems left ventricular assist device (Frazier) 1992;54:1019,CP; Reply (Burton, Phillips, & others) 1992;54:1019–20,CP

Heart atrium

Left atrial isolation associated with mitral valve operations (Graffigna, Pagani, & others) 1992;54:1093–8*

Optimal approach to the mitral valve: dissection of the interatrial groove (Larbalestier, Chard, & Cohn) 1992;54:1186–8*

Surgical implications of juxtaposed atrial appendages and the associated anomalies (Leu, Chiu, & others) 1992;54:134–6*

Heart conduction system

Accessory atrioventricular node and bundle: a cause of antidromic reentry tachycardia (Sealy, Kopelman, & Murphy) 1992;54:306–10*

Morphology of the posterior junctional area in atrioventricular septal defects (Ho, Gerlis, & others) 1992;54:264–70*

Heart defects, congenital

Absent pulmonary valve syndrome: operation in infants with airway obstruction (Watterson, Malm, & others) 1992;54:1116–9*

Accessory atrioventricular node and bundle: a cause of antidromic reentry tachycardia (Sealy, Kopelman, & Murphy) 1992;54:306–10*

Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation (Vouhé, Tamisier, & others) 1992;54:621–7*

Atrioventricular pacing in congenital heart disease (Kratz, Gillette, & others) 1992;54:485–9*

Balloon angioplasty in the treatment of aortic coarctation (Ergina & Tchervenkov) 1992;54:599–600,CP; Reply (Rao & Chopra) 1992;54:600–2,CP

Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR

Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR

Coarctation of the aorta in infants: does the aortic arch grow after repair? (Myers, McConnell, & Waldhausen) 1992;54:869–75*

Coarctation repair in neonates with subclavian-sparing advancement flap (Sharma, Calderon, & Ott) 1992;54:137–41*

Complete cure after a seemingly unsuccessful operation for Wolff-Parkinson-White syndrome (Rakovec, Brecelj, & Zupan) 1992;54:1203–5,CR

Congenital aortic stenosis and patent ductus arteriosus in the adult (Glower, Bashore, & Spritzer) 1992;54:368–70,CR

Congenital malformations of the coronary arteries: the Texas Heart Institute experience (Fernandes, Kadivar, & others) 1992;54:732–40*

Damus-Stansel-Kaye procedure: technical modifications (Laks, Gates, & others) 1992;54:169–72,HW

Extracardiac total cavopulmonary connection (Laschinger, Ringel, & others) 1992;54:371–3,CR

Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation (Ziomek, Harrell, & others) 1992;54:861–8*

Fontan procedure for hypoplastic left heart syndrome (Norwood, Jacobs, & Murphy) 1992;54:1025–30*

Intraoperative echocardiographic diagnosis of previously unrecognized cor triatriatum (Hogue, Barzilai, & others) 1992;54:562–3,CR

The learning curve for intraoperative echocardiography during congenital heart surgery (Ungerleider, Greeley, & others) 1992;54:691–8*

Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis (Leung, Lee, & others) 1992;54:523–7*

New surgical technique for total-defect aortopulmonary window (Matsuki, Yagihara, & others) 1992;54:991–2,HW

Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR

Pediatric lung transplantation for pulmonary hypertension and congenital heart disease (Spray, Mallory, & others) 1992;54:216–25*

Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR

Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54:164–5,HW

A staged expanding pulmonary artery band (Warren, Heath, & Brand) 1992;54:240–3*

Surgical implications of juxtaposed atrial appendages and the associated anomalies (Leu, Chiu, & others) 1992;54:134–6*

Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries (Yoshimura, Yamaguchi, & others) 1992;54:573–5,CR

Tetralogy of Fallot: favorable outcome of nonneonatal transatrial, transpulmonary repair (Karl, Sano, & others) 1992;54:903–7*

Total correction of transposition of great arteries with atrioventricular septal defect (Kumar, Prabhakar, & others) 1992;54:989–90,CR

Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*

Heart failure, congestive

Abrupt cardiac failure using a right VAD in the presence of a tricuspid valve prosthesis (Griffin & Dark) 1992;54:1023–4,CP

Comparison of 180-degree and 360-degree skeletal muscle nerve cuff electrodes (Letsou, Hogan, & others) 1992;54:925–31*

Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*

Production and reversibility of right ventricular hypertrophy and right heart failure in dogs (Hsieh, Mishkel, & others) 1992;54:104–10*

Heart function
Isolated biventricular working rat heart preparation (Demmy, Magovern, & Kao) 1992;54:915–20*
Heart injuries
Penetrating cardiac trauma (Ivatury & Rohman) 1992;54:1247–8,CP; Reply (Knott-Craig) 1992;54:1248,CP
Heart-lung transplantation
Acute rejection of lung allografts with various immunosuppressive protocols (Griffith, Hardesty, & others) 1992;54:846–51*
A prostacyclin analogue reduces free radical generation in heart-lung transplantation (Takeuchi, Suzuki, & others) 1992;54:327–32*
Heart neoplasms
Clarence Crafoord and the first successful resection of a cardiac myxoma (Chitwood) 1992;54:997–8,CL
Heart septal defects
Morphology of the posterior junctional area in atrioventricular septal defects (Ho, Gerlis, & others) 1992;54:264–70*
Total correction of transposition of great arteries with atrioventricular septal defect (Kumar, Prabhakar, & others) 1992;54:989–90,CR
Heart septal defects, atrial
Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR
Heart septal defects, ventricular
Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR
Postinfarct ventricular septal defect repair: effect of coronary artery bypass grafting (Muehrcke, Daggett, & others) 1992;54:876–83*
Surgical treatment of postinfarction ventricular septal defect with aortic stenosis (Boglioli, Traill, & others) 1992;54:1209–11,CR
Heart surgery
Acadesine (AICA-riboside) improves postischemic cardiac recovery (Bolling, Groh, & others) 1992;54:93–8*
Acute pulmonary edema in closed mitral commissurotomy (Tewari & Kumar) 1992;54:191,CP
Aortic valve repair (Cosgrove) 1992;54:1014–5,KR
Aprotinin treatment during open heart operation in a patient with severe thrombocytopenia (Deviri, Izhar, & others) 1992;54:1018–9,CP
Bilateral adrenal hemorrhage after an open heart operation (Ting, Nosher, & others) 1992;54:357–8,CR
Cardiac valve replacement in patients infected with the human immunodeficiency virus (Bräu, Esposito, & Simberkoff) 1992;54:552–4,CR
Coarctation repair in neonates with subclavian-sparing advancement flap (Sharma, Calderon, & Ott) 1992;54:137–41*
Combined maze procedure and septal myectomy in a septuagenarian (Blitz, McLoughlin, & others) 1992;54:364–5,CR
Combined superior and right lateral left atriotomy with division of the superior vena cava for exposure of the mitral valve (Barner) 1992;54:594,UP
Complete cure after a seemingly unsuccessful operation for Wolff-Parkinson-White syndrome (Rakovec, Brecelj, & Zupan) 1992;54:1203–5,CR
Concomitant cardiac and pulmonary operation: the role of cardiopulmonary bypass (Ulicny, Schmelzer, & others) 1992;54:289–95*
Damus-Stansel-Kaye procedure: technical modifications (Laks, Gates, & others) 1992;54:169–72,HW
Does a posterior aneurysm increase the risk of endocardial resection? (Kron, Kern, & others) 1992;54:617–20*
Electrophysiologic study of dysrhythmias after atrial operations in dogs (Tamiya, Yamashiro, & others) 1992;54:717–24*
Extended approach to the mitral valve (Sampathkumar) 1992;54:596–7,CP; Reply (Guiraudon) 1992;54:597–8,CP
Extracorporeal membrane oxygenation for cardiac failure after congenital heart operation (Ziomek, Harrell, & others) 1992;54:861–8*
Factors affecting mitral valve reoperation in 317 survivors after mitral valve reconstruction (Fernandez, Joyce, & others) 1992;54:440–8*
Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery (Menasché, Fleury, & Piwnica) 1992;54:392–3,UP
Fontan procedure for hypoplastic left heart syndrome (Norwood, Jacobs, & Murphy) 1992;54:1025–30*
Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*
Hemodynamic effects of pericardial closure (Sampathkumar) 1992;54:1023,CP; Reply (Hunter & Angelini) 1992;54:1023,CP
Hemolysis after open heart operations (Golino, Stassano, & Spampinato) 1992;54:1246–7,CP; Reply (Okita & Miki) 1992;54:1247,CP
Influence of β_1-blockade on myocardial substrates early after coronary operation (Wesslén, van der Linden, & others) 1992;54:1151–8*
Intraaortic balloon counterpulsation: patterns of usage and outcome in cardiac surgery patients (Creswell, Rosenbloom, & others) 1992;54:11–20*
Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW
Ischemic mitral valve repair (Cheng) 1992;54:190–1,CP
Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*
The learning curve for intraoperative echocardiography during congenital heart surgery (Ungerleider, Greeley, & others) 1992;54:691–8*
Left atrial isolation associated with mitral valve operations (Graffigna, Pagani, & others) 1992;54:1093–8*
Long-term follow-up results after reconstruction of the mitral valve by leaflet advancement (Hisatomi, Isomura, & others) 1992;54:271–5*
Long-term results of the Ivalon baffle mitral valve repair (Odell, Schurek, & others) 1992;54:283–5*
Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW
Mitral valve repair in patients with endomyocardial fibrosis (Uva, Jebara, & others) 1992;54:89–92*
Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis (Leung, Lee, & others) 1992;54:523–7*
A new idea (Neptune) 1992;54:188,CP
Optimal approach to the mitral valve: dissection of the interatrial groove (Larbalestier, Chard, & Cohn) 1992;54:1186–8*
Pericardioplasty (Schmidt, Wood, & Vyhmeister) 1992;54:584–5,HW
Postcardiotomy centrifugal mechanical ventricular support (Golding, Crouch, & others) 1992;54:1059–64*

Postinfarct ventricular septal defect repair: effect of coronary artery bypass grafting (Muehrcke, Daggett, & others) 1992;54:876–83*

Prolonged open sternotomy and delayed sternal closure after cardiac operations (Furnary, Magovern, & others) 1992;54:233–9*

A randomized study of the systemic effects of warm heart surgery (Christakis, Koch, & others) 1992;54:449–59*

Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR

Repairing the degenerative anterior mitral leaflet (Alvarez, Teoh, & Deal) 1992;54:1229–30,HW

Safety and efficacy of autologous blood donation before elective aortic valve operation (Dzik, Fleisher, & others) 1992; 54:1177–81*

Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW

Subcutaneous use of erythropoietin in heart surgery (Watanabe, Fuse, & others) 1992;54:479–84*

Surgical management of infective endocarditis in children (Citak, Rees, & Mavroudis) 1992;54:755–60*

Surgical treatment for ectopic atrial tachycardia (Graffigna, Vigano, & others) 1992;54:338–43*

Surgical treatment of postinfarction ventricular septal defect with aortic stenosis (Boglioli, Traill, & others) 1992;54:1209–11,CR

Surgically created Wolff-Parkinson-White syndrome after Fontan operation (Razzouk, Gow, & others) 1992;54:974–7,CR

Tetralogy of Fallot: favorable outcome of nonneonatal transatrial, transpulmonary repair (Karl, Sano, & others) 1992; 54:903–7*

Thoracic aortic operations in patients aged 70 years or older (Tabayashi, Ohmi, & others) 1992;54:279–82*

Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*

Heart transplantation

Aneurysm of the ascending aorta after cardiac transplantation (Defraigne, Vahdat, & others) 1992;54:983–4,CR

Attenuation of waiting time mortality with heterotopic heart transplantation (Sekela, Smart, & others) 1992;54:547–51*

Cardiac retransplantation: a viable option? (Karwande, Ensley, & others) 1992;54:840–5*

Clinical trial of FK 506 immunosuppression in adult cardiac transplantation (Armitage, Kormos, & others) 1992;54:205–11*

Coronary artery bypass grafting nine years after cardiac transplantation (Dunning, Kendall, & others) 1992;54:571–2,CR

Heterotopic heart transplantation and recipient heart operation in ischemic heart disease (Ridley, Khaghani, & others) 1992;54:333–7*

Heterotopic transplantation: is it a viable alternative? (Baumgartner) 1992;54:401–2,ED

Improved myocardial ischemic tolerance by contractile inhibition with 2,3-butanedione monoxime (Stringham, Paulsen, & others) 1992;54:852–60*

Mediastinitis in heart transplantation (Karwande, Renlund, & others) 1992;54:1039–45*

Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance (Karck, Vivi, & others) 1992;54:348–51*

Total orthotopic heart transplantation: an alternative to the standard technique (Kendall, Ciulli, & others) 1992;54:187,CP; Reply (Dreyfus) 1992;54:187–8,CP

True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient (Baldwin, Klima, & others) 1992;54:978–9,CR

Use of epicardial electrocardiograms for detecting cardiac allograft rejection (Irwin, Binco, & others) 1992;54:669–75*

Heart valve diseases

Central cyanosis due to prominence of the eustachian and thebesian valves (Raffa, Al-Ibrahim, & others) 1992;54:159–60,CR

Safety and efficacy of autologous blood donation before elective aortic valve operation (Dzik, Fleisher, & others) 1992; 54:1177–81*

Heart valve prosthesis

Abrupt cardiac failure using a right VAD in the presence of a tricuspid valve prosthesis (Griffin & Dark) 1992;54:1023–4,CP

Approach for insertion of aortic composite valve grafts (Svensson) 1992;54:376–8,HW

Cardiac valve replacement in patients infected with the human immunodeficiency virus (Bräu, Esposito, & Simberkoff) 1992;54:552–4,CR

Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin (Lamarra, Azzu, & Kulatilake) 1992;54:361–3,CR

Clinical and hemodynamic assessment of the Hancock II bioprosthesis (David, Armstrong, & Sun) 1992;54:661–8*

Clinical and hemodynamic evaluation of the 19-mm Carpentier-Edwards supraannular aortic valve (Kallis, Sneddon, & others) 1992;54:1182–5*

Composite valve graft replacement of the proximal aorta: comparison of techniques in 348 patients (Svensson, Crawford, & others) 1992;54:427–39*

Early structural deterioration with the Mitroflow pericardial xenograft in the mitral position (Bernal, Rabasa, & others) 1992;54:152–4,CR

Ionescu-Shiley valve failure I: experience with 125 standard-profile explants (Walley, Keon, & others) 1992;54:111–6*

Ionescu-Shiley valve failure II: experience with 25 low-profile explants (Walley, Keon, & others) 1992;54:117–23*

Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*

Long-term results of St. Jude medical valve in the tricuspid position (Singh, Feng, & Sanofsky) 1992;54: 538–40*

The Meadox-Gabbay pericardial xenograft: failure of the unicusp principle (Bortolotti, Ius, & others) 1992;54:952–8*

Mitral valve replacement: randomized trial of St. Jude and Medtronic-Hall prostheses (Fiore, Naunheim, & others) 1992;54:68–73*

Replacement of the valvular prosthesis in a patient with a Bentall procedure (Panos, Teoh, & others) 1992;54:555–6,CR

Rereplacement of the mitral valve with representation of the subvalvular apparatus (Olinger) 1992;54:188–90,CP

Retrograde disc escape in a Harken mitral valve prosthesis (Berger) 1992;54:394,CP; Reply (Otero-Coto) 1992:54;394–5,CP

Simplified correction of outflow obstruction after mitral valve replacement (Reed & Iverson) 1992;54:985–6,CR

Stentless porcine and pericardial valve in aortic position (Casabona, De Paulis, & others) 1992;54:681–5*

Heart valve prosthesis (cont'd)
Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries (Yoshimura, Yamaguchi, & others) 1992;54:573–5,CR
Heart ventricle
Acute severe postischemic myocardial depression reversed by triiodothyronine (Holland, Brown, & Clark) 1992;54:301–5*
Clinical cardiomyoplasty: preoperative factors associated with outcome (Furnary, Magovern, & others) 1992;54:1139–43*
Does a posterior aneurysm increase the risk of endocardial resection? (Kron, Kern, & others) 1992;54:617–20*
Isolated biventricular working rat heart preparation (Demmy, Magovern, & Kao) 1992;54:915–20*
Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*
Left ventricular diverticulum with hypertrophy of the left ventricular apex (Yamashita, Nakamura, & others) 1992; 54:761–3,CR
Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW
Production and reversibility of right ventricular hypertrophy and right heart failure in dogs (Hsieh, Mishkel, & others) 1992;54:104–10*
Repair of aortico–left ventricular tunnel associated with subpulmonary obstruction (Knott-Craig, van der Merwe, & others) 1992;54:557–9,CR
Retrograde versus antegrade cardioplegia: impact on right ventricular function (Douville, Kratz, & others) 1992;54: 56–61*
Skeletal muscle ventricles as left atrial–aortic pumps: short-term studies (Hooper, Niinami, & others) 1992;54:316–22*
Usefulness of right ventricular indices in early diagnosis of cardiac tamponade (Jones, Izzat, & others) 1992;54:44–9*
Hemangioma
Intercostal hemangioma presenting as a chest wall tumor (Winchester, Victor, & Fry) 1992;54:145–6,CR
Hemodilution
Minimal hemodilution and optimal potassium use during normothermic aerobic arrest (Le Houerou, Singh, & others) 1992;54:815–6,CP
A new idea (Neptune) 1992;54:188,CP
Hemodynamics
Hemodynamic effects of pericardial closure (Sampathkumar) 1992;54:1023,CP; Reply (Hunter & Angelini) 1992;54: 1023,CP
Hemolysis
Hemolysis after open heart operations (Golino, Stassano, & Spampinato) 1992;54:1246–7,CP; Reply (Okita & Miki) 1992;54:1247,CP
Hemorrhage
Bilateral adrenal hemorrhage after an open heart operation (Ting, Nosher, & others) 1992;54:357–8,CR
Thromboelastogram and postoperative hemorrhage (Spiess) 1992;54:810–1,CP (Tuman, McCarthy, & Ivankovich) 1992; 54:811–2,CP; (Martin, Horkay, & others) 1992;54:812–3,CP; Reply (Lin & Wang) 1992;54:813,CP
Hepatic artery
Esophagogastrectomy and the variant left hepatic artery (Hemming, Finley, & others) 1992;54:166–8,HW
Hernia, diaphragmatic
Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia (Carroll, Kramer, & others) 1992;54:1212–3,CR
Histoplasmosis
Clinical manifestation of mediastinal fibrosis and histoplasmosis (Mathisen & Grillo) 1992;54:1053–8*
How to do it
Approach for insertion of aortic composite valve grafts (Svensson) 1992;54:376–8,HW
Bilateral anterior thoracotomy for automatic implantable cardioverter defibrillator placement in patients with previous sternotomy (Karwande & Rowles) 1992;54:791–3,HW
Cervical esophago-esophageal anastomosis (Fraser & Heitmiller) 1992;54:384–6,HW
Damus-Stansel-Kaye procedure: technical modifications (Laks, Gates, & others) 1992;54:169–72,HW
Directed atraumatic coronary sinus cannulation for retrograde cardioplegia administration (Aldea, Connelly, & others) 1992;54:789–90,HW
Esophagogastrectomy and the variant left hepatic artery (Hemming, Finley, & others) 1992;54:166–8,HW
Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW
Limited vertical skin incision for median sternotomy (Tatebe, Eguchi, & others) 1992;54:787–8,HW
Management of aortic cannulation site blowouts (Szentpetery) 1992;54:582–3,HW
Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW
Method of single-lung transplantation in the absence of a left atrial cuff (Hammond, Franco, & Baldwin) 1992;54:379–80,HW
Modified urinary collecting bags for prolonged underwater chest drainage (Bar-El, Lieberman, & Yellin) 1992;54:995–6,HW
New side-holed sheath for intraaortic balloon pumping to maintain limb perfusion (Satoh, Kobayashi, & others) 1992;54:794–6,HW
New surgical technique for total-defect aortopulmonary window (Matsuki, Yagihara, & others) 1992;54:991–2,HW
New surgical technique for type B aortic interruption (Kumar, Prabhakar, & others) 1992;54:797–9,HW
Newly developed holder for a right-angled metal venous cannula (Watanabe, Abe, & others) 1992;54:993–4,HW
Pericardioplasty (Schmidt, Wood, & Vyhmeister) 1992;54:584–5,HW
Permanent pacemaker implantation in premature infants less than 2,000 grams of body weight (Ohmi, Tofukuji, & others) 1992;54:1223–5,HW
Placement of an endotracheal tube in the short tracheal stump (Pellegrini, Mucci, & others) 1992;54:578–9,HW
Repairing the degenerative anterior mitral leaflet (Alvarez, Teoh, & Deal) 1992;54:1229–30,HW
Replacement of paracorporeal ventricular assist devices (Lohmann, McBride, & others) 1992;54:1226–7,HW
Right internal mammary artery extended with an inferior epigastric artery for circumflex and right coronary bypass (Buche, Schroeder, & others) 1992;54:381–3,HW
Safe intraaortic balloon pump placement through the ascending aorta using transesophageal ultrasound (Kaplan, Weiman, & others) 1992;54:374–5,HW
Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW
Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54: 164–5,HW

Subfascial implantation of implantable cardioverter defibrillator generator (Shahian, Williamson, & others) 1992;54:173–4,HW
Videothoracoscopic enucleation of esophageal leiomyoma (Bardini, Segalin, & others) 1992;54:576–7,HW

Human immunodeficiency virus
Cardiac valve replacement in patients infected with the human immunodeficiency virus (Brău, Esposito, & Simberkoff) 1992;54:552–4,CR

Hyperemia
Reactive hyperemia in the nonused internal mammary artery after median sternotomy (van Son, Skotnicki, & others) 1992;54:130–3*

Hyperglycemia
Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest (Anderson, Siegman, & others) 1992;54:1126–30*

Hypertension
Multicenter trial of automated nitroprusside infusion for postoperative hypertension (Chitwood, Cosgrove, & others) 1992;54:517–22*

Hypertension, pulmonary
Pediatric lung transplantation for pulmonary hypertension and congenital heart disease (Spray, Mallory, & others) 1992;54:216–25*
Production and reversibility of right ventricular hypertrophy and right heart failure in dogs (Hsieh, Mishkel, & others) 1992;54:104–10*
Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW

Hypertrophy
Left ventricular diverticulum with hypertrophy of the left ventricular apex (Yamashita, Nakamura, & others) 1992;54:761–3,CR
Production and reversibility of right ventricular hypertrophy and right heart failure in dogs (Hsieh, Mishkel, & others) 1992;54:104–10*

Hypoplastic left heart syndrome
Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR

Hypothermia, induced
Barbiturates impair cerebral metabolism during hypothermic circulatory arrest (Siegman, Anderson, & others) 1992;54:1131–6*
Cerebral blood flow and metabolism in hypothermic circulatory arrest (Mezrow, Sadeghi, & others) 1992;54:609–16*
Hyperglycemia increases cerebral intracellular acidosis during circulatory arrest (Anderson, Siegman, & others) 1992;54:1126–30*
Hypothermic thoracic and thoracoabdominal aneurysm operation: a central cannulation technique (Westaby) 1992;54:253–8*
Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance (Karck, Vivi, & others) 1992;54:348–51*
Profound hypothermia and circulatory arrest (Baudet) 1992;54:596,CP; Reply (Rainer) 1992;54:596,CP
Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms (Yamashita, Nakamura, & others) 1992;54:566–8,CR
Temperature monitoring during CPB in infants: does it predict efficient brain cooling? (Kern, Jonas, & others) 1992;54:749–54*

Immunoglobulins
Pneumatocele complicating hyperimmunoglobulin E syndrome (Job's syndrome) (Shamberger, Wohl, & others) 1992;54:1206–8,CR

Immunosuppression
Acute rejection of lung allografts with various immunosuppressive protocols (Griffith, Hardesty, & others) 1992;54:846–51*
Clinical trial of FK 506 immunosuppression in adult cardiac transplantation (Armitage, Kormos, & others) 1992;54:205–11*

Incision
Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW
Limited vertical skin incision for median sternotomy (Tatebe, Eguchi, & others) 1992;54:787–8,HW

Infant
Absent pulmonary valve syndrome: operation in infants with airway obstruction (Watterson, Malm, & others) 1992;54:1116–9*
Coarctation of the aorta in infants: does the aortic arch grow after repair? (Myers, McConnell, & Waldhausen) 1992;54:869–75*
Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR
Pulmonary artery sling (Pawade, de Leval, & others) 1992;54:967–70*
Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy (Ziemer, Heinemann, & others) 1992;54:971–3,CR
Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW
Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries (Yoshimura, Yamaguchi, & others) 1992;54:573–5,CR
Temperature monitoring during CPB in infants: does it predict efficient brain cooling? (Kern, Jonas, & others) 1992;54:749–54*
Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*

Infant, newborn
Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR
Coagulation defects in neonates during cardiopulmonary bypass (Kern, Morana, & others) 1992;54:541–6*
Coarctation repair in neonates with subclavian-sparing advancement flap (Sharma, Calderon, & Ott) 1992;54:137–41*
Fontan procedure for hypoplastic left heart syndrome (Norwood, Jacobs, & Murphy) 1992;54:1025–30*
Myocardial protection of neonatal heart by cardioplegic solution with recombinant human superoxide dismutase (Tatebe, Nakazawa, & others) 1992;54:124–9*
New surgical technique for total-defect aortopulmonary window (Matsuki, Yagihara, & others) 1992;54:991–2,HW
Newly developed holder for a right-angled metal venous cannula (Watanabe, Abe, & others) 1992;54:993–4,HW
Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54:164–5,HW
A staged expanding pulmonary artery band (Warren, Heath, & Brand) 1992;54:240–3*

Infant, newborn (cont'd)
Tetralogy of Fallot: favorable outcome of nonneonatal transatrial, transpulmonary repair (Karl, Sano, & others) 1992; 54:903–7*
Infant, premature
Permanent pacemaker implantation in premature infants less than 2,000 grams of body weight (Ohmi, Tofukuji, & others) 1992;54:1223–5,HW
Innominate artery
Anterior mediastinal tracheostomy with and without cervical exenteration (Orringer) 1992;54:628–37*
Insulin
Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*
Intercostal muscles
Intercostal hemangioma presenting as a chest wall tumor (Winchester, Victor, & Fry) 1992;54:145–6,CR
Internal mammary–coronary artery anastomosis
Bioassay of EDRF from internal mammary arteries: implications for early and late bypass patency (Pearson, Evora, & Schaff) 1992;54:1078–84*
Competitive flow from a fully patent coronary artery does not limit acute mammary graft flow (Spence, Lust, & others) 1992;54:21–6*
Low-dose aprotinin in internal mammary artery bypass operations contributes to important blood saving (Schönberger, Everts, & others) 1992;54:1172–6*
Right internal mammary artery extended with an inferior epigastric artery for circumflex and right coronary bypass (Buche, Schroeder, & others) 1992;54:381–3,HW
Intraaortic balloon pumping
Benefits of combined balloon pumping and percutaneous cardiopulmonary bypass (Phillips, Zeff, & others) 1992;54: 908–10*
Experience in 100 transthoracic balloon pumps (Hazelrigg, Auer, & Seifert) 1992;54:528–32*
Intraaortic balloon counterpulsation: patterns of usage and outcome in cardiac surgery patients (Creswell, Rosenbloom, & others) 1992;54:11–20*
Is use of the intraaortic balloon pump in octogenarians justified? (Sisto, Hoffman, & others) 1992;54:507–11*
New side-holed sheath for intraaortic balloon pumping to maintain limb perfusion (Satoh, Kobayashi, & others) 1992;54:794–6,HW
Safe intraaortic balloon pump placement through the ascending aorta using transesophageal ultrasound (Kaplan, Weiman, & others) 1992;54:374–5,HW
Intraoperative complications
Pericardial repair of a tracheal laceration during transhiatal esophagectomy (Gorenstein, Abel, & Patterson) 1992;54: 784–6,CR
Intubation
Palliative intubation for dysphagia (Wetstein) 1992;54:813–4,CP; Reply (Liakakos, Ohri, & others) 1992;54:814,CP
Placement of an endotracheal tube in the short tracheal stump (Pellegrini, Mucci, & others) 1992;54:578–9,HW
Iodine
The blue man phenomenon (Mitchell, Saunders, & others) 1992;54:814,CP
Ischemia
Acadesine (AICA-riboside) improves postischemic cardiac recovery (Bolling, Groh, & others) 1992;54:93–8*
Acute severe postischemic myocardial depression reversed by triiodothyronine (Holland, Brown, & Clark) 1992;54:301–5*
Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung (Yamashita, Oobo, & others) 1992;54:921–4*
Improved myocardial ischemic tolerance by contractile inhibition with 2,3-butanedione monoxime (Stringham, Paulsen, & others) 1992;54:852–60*
Ischemic mitral valve repair (Cheng) 1992;54:190–1,CP
Management of severe bronchial ischemia after bilateral sequential lung transplantation (Oturanlar, Klepetko, & others) 1992;54:1221–2,CR
Nicardipine: myocardial protection in isolated working hearts (Mitchell, DeBoer, & others) 1992;54:712–6*
Normothermic cardioplegia: is aortic cross-clamping still synonymous with myocardial ischemia? (Menasché, Peynet, & others) 1992;54:472–8*

Key references
Aortic valve repair (Cosgrove) 1992;54:1014–5,KR
Dynamic cardiomyoplasty (Chiu) 1992;54:592–3,KR
Physician payment reform: a bibliography (Miller) 1992;54:184–5,KR

Laser surgery
Radical laser segmentectomy for T1 N0 lung cancer (Kodama, Doi, & others) 1992;54:1193–5*
Leiomyoma
Videothoracoscopic enucleation of esophageal leiomyoma (Bardini, Segalin, & others) 1992;54:576–7,HW
Ligation
Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54: 164–5,HW
Liposarcoma
Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia (Carroll, Kramer, & others) 1992;54:1212–3,CR
Lung
Internal mammary artery to lung parenchyma fistula (Wood) 1992;54:603,CP; Reply (Blanche) 1992;54:603,CP
Role of open lung biopsy in diagnosing pulmonary complications of AIDS (Trachiotis, Hafner, & others) 1992;54:898–902*
Lung diseases
Open lung biopsy for diffuse infiltrative lung disease (Chechani, Landreneau, & Shaikh) 1992;54:296–300*
Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR
Pleuropulmonary aspergilloma: clinical spectrum and results of surgical treatment (Massard, Roeslin, & others) 1992;54: 1159–64*
Pneumatocele complicating hyperimmunoglobulin E syndrome (Job's syndrome) (Shamberger, Wohl, & others) 1992;54:1206–8,CR
Thoracoscopic lung biopsy (McKeown, Conant, & Hubbell) 1992;54:490–2*
Thoracoscopic resection of 85 pulmonary lesions (Landreneau, Hazelrigg, & others) 1992;54:415–20*
Videothoracoscopic wedge excision of the lung (Miller, Allen, & others) 1992;54:410–4*
Lung neoplasms
Better salvage in non–small cell lung cancer (Chambers) 1992; 54:399–400,CP
Bronchial carcinoid tumors: a retrospective analysis of 126 patients (Harpole, Feldman, & others) 1992;54:50–5*

Imaged thoracic lobectomy: should it be done? (Lewis, Sisler, & Caccavale) 1992;54:80–3*
A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer (Nakahara, Miyoshi, & Nakagawa) 1992;54:1016–7,UP
Multimodal therapy of small cell lung cancer in TNM stages I through IIIa (Müller, Salzer, & others) 1992;54:493–7*
Primary lung cancer in young patients: a study of 82 surgically treated patients (Icard, Regnard, & others) 1992;54:99–103*
Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*
Pulmonary pseudotumor (Fadhli) 1992;54:1246,CP
Radical laser segmentectomy for T1 N0 lung cancer (Kodama, Doi, & others) 1992;54:1193–5*
Results of operation without adjuvant therapy in the treatment of small cell lung cancer (Shah, Thompson, & Goldstraw) 1992;54:498–501*
Surgical treatment for higher stage non–small cell lung cancer (Van Raemdonck, Schneider, & Ginsberg) 1992;54:999–1013,CV
Survival after resection of stage II non–small cell lung cancer (Martini, Burt, & others) 1992;54:460–6*

Lung surgery
Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
Radical laser segmentectomy for T1 N0 lung cancer (Kodama, Doi, & others) 1992;54:1193–5*

Lung transplantation
Acute rejection of lung allografts with various immunosuppressive protocols (Griffith, Hardesty, & others) 1992;54:846–51*
Double-lung transplantation for cystic fibrosis (Shennib, Noirclerc, & others) 1992;54:27–32*
Double-lung transplantation using donor lungs with a right tracheal bronchus (Brichon, Blin, & others) 1992;54:777–8,CR
Early cellular events in the lung allograft (Adoumie, Serrick, & others) 1992;54:1071–7*
Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung (Yamashita, Oobo, & others) 1992;54:921–4*
Management of severe bronchial ischemia after bilateral sequential lung transplantation (Oturanlar, Klepetko, & others) 1992;54:1221–2,CR
Method of single-lung transplantation in the absence of a left atrial cuff (Hammond, Franco, & Baldwin) 1992;54:379–80,HW
Pediatric lung transplantation for pulmonary hypertension and congenital heart disease (Spray, Mallory, & others) 1992;54:216–25*
Predictive criteria for the need of extracorporeal circulation in single-lung transplantation (Hirt, Haverich, & others) 1992;54:676–80*
Production and reversibility of right ventricular hypertrophy and right heart failure in dogs (Hsieh, Mishkel, & others) 1992;54:104–10*
Pulmonary "twinning" procedure: use of lungs from one donor for single-lung transplantation in two recipients (Haydock, Low, & others) 1992;54:1189–92*
Role of the bronchial arteries in lung function (Ventemiglia) 1992;54:395–6,CP; Reply (Schreinemakers, De Leyn, & others) 1992;54:396–7,CP; Reply (Couraud, Baudet, & others) 1992;54:397,CP
Vascular and interstitial effect of University of Wisconsin solution on canine lung (Unruh) 1992;54:1168–71*

Lymph nodes
Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*
Survival after resection of stage II non–small cell lung cancer (Martini, Burt, & others) 1992;54:460–6*

Lymphoma
Tracheoesophageal fistula after chemotherapy for lymphoma (Sharpe, Sendegeya, & others) 1992;54:366–7,CR

Malignant carcinoid syndrome
Surgical management of carcinoid heart disease (Aldrete) 1992;54:598,CP; Reply (Davis) 1992;54:598,CP

Mediastinal cyst
Aneurysm of coronary arteriovenous fistula presenting as a calcified mediastinal mass (Okita, Miki, & others) 1992;54:771–3,CR

Mediastinal diseases
Clinical manifestation of mediastinal fibrosis and histoplasmosis (Mathisen & Grillo) 1992;54:1053–8*
Mediastinal window: a cause of simultaneous bilateral spontaneous pneumothorax (Juvonen, Lepojärvi, & others) 1992;54:560–1,CR

Mediastinal neoplasms
Exocrine pancreatic function in mediastinal teratomata: an aid to preoperative diagnosis? (Kallis, Treasure, & others) 1992;54:741–3*
Thoracoscopic resection of an anterior mediastinal tumor (Landreneau, Dowling, & others) 1992;54:142–4,CR

Mediastinitis
Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis (Lagerstrom, Mitchell, & others) 1992;54:764–5,CR
Mediastinitis in heart transplantation (Karwande, Renlund, & others) 1992;54:1039–45*
Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis (Smith & Goldstein) 1992;54:766–8,CR

Mediastinum
Anterior mediastinal tracheostomy with and without cervical exenteration (Orringer) 1992;54:628–37*
Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*
Survival after resection of stage II non–small cell lung cancer (Martini, Burt, & others) 1992;54:460–6*

Mesothelioma
Extrapleural pneumonectomy in the treatment of malignant pleural mesothelioma (Sugarbaker, Mentzer, & Strauss) 1992;54:941–6*
Giant intrapericardial solitary fibrous tumor (Bortolotti, Calabrò, & others) 1992;54:1219–20,CR

Metabolism
Barbiturates impair cerebral metabolism during hypothermic circulatory arrest (Siegman, Anderson, & others) 1992;54:1131–6*
Cerebral blood flow and metabolism in hypothermic circulatory arrest (Mezrow, Sadeghi, & others) 1992;54:609–16*

Metoprolol
Influence of β_1-blockade on myocardial substrates early after coronary operation (Wesslén, van der Linden, & others) 1992;54:1151–8*

Mitral valve
Acute pulmonary edema in closed mitral commissurotomy (Tewari & Kumar) 1992;54:191,CP

Mitral valve (cont'd)
- Combined superior and right lateral left atriotomy with division of the superior vena cava for exposure of the mitral valve (Barner) 1992;54:594,UP
- Extended approach to the mitral valve (Sampathkumar) 1992;54:596–7,CP; Reply (Guiraudon) 1992;54:597–8,CP
- Factors affecting mitral valve reoperation in 317 survivors after mitral valve reconstruction (Fernandez, Joyce, & others) 1992;54:440–8*
- Ischemic mitral valve repair (Cheng) 1992;54:190–1,CP
- Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*
- Left atrial isolation associated with mitral valve operations (Graffigna, Pagani, & others) 1992;54:1093–8*
- Long-term follow-up results after reconstruction of the mitral valve by leaflet advancement (Hisatomi, Isomura, & others) 1992;54:271–5*
- Long-term results of the Ivalon baffle mitral valve repair (Odell, Schurek, & others) 1992;54:283–5*
- Mechanical support for intraventricular decompression in repair of left ventricular disruption (Baldwin & Cooley) 1992;54:175–6,HW
- Mitral valve repair in patients with endomyocardial fibrosis (Uva, Jebara, & others) 1992;54:89–92*
- Optimal approach to the mitral valve: dissection of the interatrial groove (Larbalestier, Chard, & Cohn) 1992;54:1186–8*
- Repairing the degenerative anterior mitral leaflet (Alvarez, Teoh, & Deal) 1992;54:1229–30,HW
- Simplified correction of outflow obstruction after mitral valve replacement (Reed & Iverson) 1992;54:985–6,CR

Muscles
- Skeletal muscle ventricles as left atrial–aortic pumps: short-term studies (Hooper, Niinami, & others) 1992;54:316–22*

Myocardial diseases
- Acadesine (AICA-riboside) improves postischemic cardiac recovery (Bolling, Groh, & others) 1992;54:93–8*
- Acute severe postischemic myocardial depression reversed by triiodothyronine (Holland, Brown, & Clark) 1992;54:301–5*

Myocardial infarction
- Effect of delay in retroperfusion therapy on infarct size reduction (Feindel, Sandhu, & others) 1992;54:1120–5*
- Surgical treatment of postinfarction ventricular septal defect with aortic stenosis (Boglioli, Traill, & others) 1992;54:1209–11,CR

Myocardial reperfusion
- Myocardial protection of neonatal heart by cardioplegic solution with recombinant human superoxide dismutase (Tatebe, Nakazawa, & others) 1992;54:124–9*

Myocardial revascularization
- Aprotinin therapy for reoperative myocardial revascularization: a placebo-controlled study (Cosgrove, Heric, & others) 1992;54:1031–8*
- Considerations in the skeletonization technique of internal thoracic artery dissection (Cunningham, Gharavi, & others) 1992;54:947–51*
- Coronary artery bypass using internal mammary artery branches (Morin, Hedderich, & others) 1992;54:911–4*
- Device-supported myocardial revascularization: safe help for sick hearts (Sweeney & Frazier) 1992;54:1065–70*
- Internal mammary artery to lung parenchyma fistula (Wood) 1992;54:603,CP; Reply (Blanche) 1992;54:603,CP
- Modified technique of internal mammary artery harvest (Sirivella, Gielchinsky, & Parsonnet) 1992;54:190,CP; Reply (John, Edmondson, & Rees) 1992;54:190,CP
- Reactive hyperemia in the nonused internal mammary artery after median sternotomy (van Son, Skotnicki, & others) 1992;54:130–3*
- Retrograde versus antegrade cardioplegia: impact on right ventricular function (Douville, Kratz, & others) 1992;54:56–61*

Myocardium
- Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*
- Improved myocardial ischemic tolerance by contractile inhibition with 2,3-butanedione monoxime (Stringham, Paulsen, & others) 1992;54:852–60*
- Influence of β_1-blockade on myocardial substrates early after coronary operation (Wesslén, van der Linden, & others) 1992;54:1151–8*
- Nicardipine: myocardial protection in isolated working hearts (Mitchell, DeBoer, & others) 1992;54:712–6*
- Normothermic cardioplegia: is aortic cross-clamping still synonymous with myocardial ischemia? (Menasché, Peynet, & others) 1992;54:472–8*
- Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance (Karck, Vivi, & others) 1992;54:348–51*

Myxoma
- Clarence Crafoord and the first successful resection of a cardiac myxoma (Chitwood) 1992;54:997–8,CL

Neoplasm metastasis
- Long-term survival after resection of pulmonary metastases from carcinoma of the breast (Lanza, Natarajan, & others) 1992;54:244–8*
- Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*
- Resectional management of thyroid carcinoma invading the airway (Grillo, Suen, & others) 1992;54:3–10*
- Tricuspid valve obstruction caused by plasmacytoma metastasis (Carrel, Linka, & Turina) 1992;54:352–4,CR

Neural conduction
- Human cardiac nerve stimulation (Murphy & Armour) 1992;54:502–6*

Nicardipine
- Nicardipine: myocardial protection in isolated working hearts (Mitchell, DeBoer, & others) 1992;54:712–6*

Nitroprusside
- Multicenter trial of automated nitroprusside infusion for postoperative hypertension (Chitwood, Cosgrove, & others) 1992;54:517–22*

Nuclear magnetic resonance
- Magnetic resonance imaging evaluation of recipient for cryopreserved aortic allograft (Kon, Link, & others) 1992;54:39–43*
- Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance (Karck, Vivi, & others) 1992;54:348–51*

Organ preservation
- Improved myocardial ischemic tolerance by contractile inhibition with 2,3-butanedione monoxime (Stringham, Paulsen, & others) 1992;54:852–60*

Osteosarcoma
- Primary bony and cartilaginous sarcomas of chest wall: results of therapy (Burt, Fulton, & others) 1992;54:226–32*

Oxygen
- Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping (Svensson, Crawford, & others) 1992;54:74–9*

Oxygen inhalation therapy
- Hyperbaric oxygen: value in management of nonhealing saphenectomy wounds (Horowitz, Portogues, & others) 1992;54:782–3,CR

Pacemaker, artificial
- Permanent pacemaker implantation in premature infants less than 2,000 grams of body weight (Ohmi, Tofukuji, & others) 1992;54:1223–5,HW

Pain, postoperative
- Lobectomy without a rib spreader (McKneally) 1992;54:2,ED

Pancreatic function
- Exocrine pancreatic function in mediastinal teratomata: an aid to preoperative diagnosis? (Kallis, Treasure, & others) 1992;54:741–3*

Paraplegia
- Intrathecal perfusion of an oxygenated perfluorocarbon prevents paraplegia after aortic occlusion (Maughan, Mohan, & others) 1992;54:818–25*

Patch
- Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW

Payment reform
- Physician payment reform: a bibliography (Miller) 1992;54:184–5,KR

Peptic ulcer
- Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty (Bégin & Sheiner) 1992;54:564–5,CR

Perfusion
- Effect of delay in retroperfusion therapy on infarct size reduction (Feindel, Sandhu, & others) 1992;54:1120–5*
- New side-holed sheath for intraaortic balloon pumping to maintain limb perfusion (Satoh, Kobayashi, & others) 1992;54:794–6,HW
- Retrograde cerebral perfusion with circulatory arrest in aortic arch aneurysms (Yamashita, Nakamura, & others) 1992;54:566–8,CR

Pericardial effusion
- Pericardioperitoneal shunt for persistent pericardial effusions: a new drainage procedure (Molnar & Jeyasingham) 1992;54:569–70,CR

Pericardial window
- Pericardial window (Weissberg) 1992;54:191–2,CP; Reply (Attar & McLaughlin) 1992;54:192,CP; Reply (Spodick) 1992;54:192,CP

Pericardium
- Giant intrapericardial solitary fibrous tumor (Bortolotti, Calabrò, & others) 1992;54:1219–20,CR
- Hemodynamic effects of pericardial closure (Sampathkumar) 1992;54:1023,CP; Reply (Hunter & Angelini) 1992;54:1023,CP
- Pericardioplasty (Schmidt, Wood, & Vyhmeister) 1992;54:584–5,HW

Peripheral nerve
- Modified retractor to prevent peripheral nerve injury (Ancalmo) 1992;54:1249,CP

Phosphorus
- Optimal level of hypothermia for prolonged myocardial protection assessed by ^{31}P nuclear magnetic resonance (Karck, Vivi, & others) 1992;54:348–51*

Photochemotherapy
- Effect of light dose on the photodynamic destruction of endobronchial tumors (McCaughan, Hawley, & others) 1992;54:705–11*

Plasmacytoma
- Tricuspid valve obstruction caused by plasmacytoma metastasis (Carrel, Linka, & Turina) 1992;54:352–4,CR

Plateletpheresis
- Plateletpheresis and transfusion practice in heart operations (Davies, Wells, & others) 1992;54:1020,CP

Pleura
- Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
- Modified urinary collecting bags for prolonged underwater chest drainage (Bar-El, Lieberman, & Yellin) 1992;54:995–6,HW

Pleural neoplasms
- Extrapleural pneumonectomy in the treatment of malignant pleural mesothelioma (Sugarbaker, Mentzer, & Strauss) 1992;54:941–6*
- Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia (Carroll, Kramer, & others) 1992;54:1212–3,CR

Pneumonectomy
- Elective pneumonectomy: factors associated with morbidity and operative mortality (Patel, Townsend, & Fountain) 1992;54:84–8*
- Extrapleural pneumonectomy in the treatment of malignant pleural mesothelioma (Sugarbaker, Mentzer, & Strauss) 1992;54:941–6*
- Postpneumonectomy syndrome: diagnosis, management, and results (Grillo, Shepard, & others) 1992;54:638–51*

Pneumothorax
- Mediastinal window: a cause of simultaneous bilateral spontaneous pneumothorax (Juvonen, Lepojärvi, & others) 1992;54:560–1,CR
- Treatment of AIDS-related bronchopleural fistula by pleurectomy (Crawford, Galloway, & others) 1992;54:212–5*

Postoperative complications
- Bilateral adrenal hemorrhage after an open heart operation (Ting, Nosher, & others) 1992;54:357–8,CR
- Concomitant cardiac and pulmonary operation: the role of cardiopulmonary bypass (Ulicny, Schmelzer, & others) 1992;54:289–95*
- Electrophysiologic study of dysrhythmias after atrial operations in dogs (Tamiya, Yamashiro, & others) 1992;54:717–24*
- Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
- Post-atherectomy coronary artery aneurysm (Cohen, Banks, & others) 1992;54:1216–8,CR
- Postpneumonectomy syndrome: diagnosis, management, and results (Grillo, Shepard, & others) 1992;54:638–51*
- Pulmonary torsion: a questionnaire survey and a survey of the literature (Wong & Goldstraw) 1992;54:286–8*
- Surgically created Wolff-Parkinson-White syndrome after Fontan operation (Razzouk, Gow, & others) 1992;54:974–7,CR
- Thromboelastogram and postoperative hemorrhage (Spiess) 1992;54:810–1,CP (Tuman, McCarthy, & Ivankovich) 1992;54:811–2,CP; (Martin, Horkay, & others) 1992;54:812–3,CP; Reply (Lin & Wang) 1992;54:813,CP

Potassium
  Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study (Girard, Quentin, & others) 1992;54:259–63*
  Minimal hemodilution and optimal potassium use during normothermic aerobic arrest (Le Houerou, Singh, & others) 1992;54:815–6,CP
Pregnancy
  Cardiopulmonary bypass in the early puerperium: possible new role for aprotinin (Lamarra, Azzu, & Kulatilake) 1992;54:361–3,CR
Prostaglandins
  Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung (Yamashita, Oobo, & others) 1992;54:921–4*
  A prostacyclin analogue reduces free radical generation in heart-lung transplantation (Takeuchi, Suzuki, & others) 1992;54:327–32*
Prosthesis
  Palliative intubation for dysphagia (Wetstein) 1992;54:813–4,CP; Reply (Liakakos, Ohri, & others) 1992;54:814,CP
Pulmonary artery
  Anomalous left coronary artery from the pulmonary artery: results of isolated aortic reimplantation (Vouhé, Tamisier, & others) 1992;54:621–7*
  Pulmonary artery sling (Pawade, de Leval, & others) 1992;54:967–70*
  Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy (Ziemer, Heinemann, & others) 1992;54:971–3,CR
  Simple method to monitor pulmonary artery pressure in infants after cardiac operations (Dietl & Torres) 1992;54:580–1,HW
  A staged expanding pulmonary artery band (Warren, Heath, & Brand) 1992;54:240–3*
  Univentricular atrioventricular connection with subaortic stenosis: a staged surgical approach (Webber, Sett, & LeBlanc) 1992;54:344–7*
Pulmonary circulation
  Carbon dioxide prevents pulmonary overcirculation in hypoplastic left heart syndrome (Jobes, Nicolson, & others) 1992;54:150–1,CR
Pulmonary valve
  Absent pulmonary valve syndrome: operation in infants with airway obstruction (Watterson, Malm, & others) 1992;54:1116–9*

Radial artery
  Revival of the radial artery for coronary artery bypass grafting (Acar, Jebara, & others) 1992;54:652–60*
Radiotherapy
  Adjuvant radiotherapy after complete resection of thymoma (Haniuda, Morimoto, & others) 1992;54:311–5*
  Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results (Parker) 1992;54:808,UP
Reperfusion injury
  Early cellular events in the lung allograft (Adoumie, Serrick, & others) 1992;54:1071–7*
  Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung (Yamashita, Oobo, & others) 1992;54:921–4*
  Electrical instability during reperfusion (Holman) 1992;54:1245–6,CP
  A prostacyclin analogue reduces free radical generation in heart-lung transplantation (Takeuchi, Suzuki, & others) 1992;54:327–32*
Report
  Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
Research
  Team approach for clinical cardiac surgery research (Canver & Fiedler) 1992;54:1244,CP
Respiration disorders
  Pleural liposarcoma presenting with respiratory distress and suspected diaphragmatic hernia (Carroll, Kramer, & others) 1992;54:1212–3,CR
Respiratory function
  A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer (Nakahara, Miyoshi, & Nakagawa) 1992;54:1016–7,UP
Retractor
  Modified retractor to prevent peripheral nerve injury (Ancalmo) 1992;54:1249,CP
Rupture
  Combined traumatic avulsion of the aortic valve and rupture of the left common carotid artery (van Heurn, Hamerlijnck, & others) 1992;54:157–8,CR
  Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Ricketts) 1992;54:177–83,CT

Saphenous vein
  Allogenic vein as a conduit for coronary artery bypass (Barner) 1992;54:817,ED
  Cryopreserved allograft veins as alternative coronary artery bypass conduits: early phase results (Laub, Muralidharan, & others) 1992;54:826–31*
  Hyperbaric oxygen: value in management of nonhealing saphenectomy wounds (Horowitz, Portogues, & others) 1992;54:782–3,CR
  Saphenous vein graft pseudoaneurysm formation after postoperative mediastinitis (Smith & Goldstein) 1992;54:766–8,CR
  True aneurysm of the saphenous vein graft stump associated with CABG in a cardiac transplant patient (Baldwin, Klima, & others) 1992;54:978–9,CR
Shock, cardiogenic
  Benefits of combined balloon pumping and percutaneous cardiopulmonary bypass (Phillips, Zeff, & others) 1992;54:908–10*
Shunt
  New side-holed sheath for intraaortic balloon pumping to maintain limb perfusion (Satoh, Kobayashi, & others) 1992;54:794–6,HW
  Pericardioperitoneal shunt for persistent pericardial effusions: a new drainage procedure (Molnar & Jeyasingham) 1992;54:569–70,CR
  Successful treatment of postoperative chylothorax using an external pleuroperitoneal shunt (Cummings, Wyatt, & others) 1992;54:276–8*
Sinus of Valsalva
  Isolated extracardiac unruptured sinus of Valsalva aneurysms (Jebara, Chauvaud, & others) 1992;54:323–6*
Skeletal muscle
  Comparison of 180-degree and 360-degree skeletal muscle nerve cuff electrodes (Letsou, Hogan, & others) 1992;54:925–31*

Skeletonization technique
Considerations in the skeletonization technique of internal thoracic artery dissection (Cunningham, Gharavi, & others) 1992;54:947–51*

The Society of Thoracic Surgeons
Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
Twenty-ninth annual meeting program, 1992;54:1250–64,AN

Southern Thoracic Surgical Association
Thirty-ninth annual meeting program, 1992;54:604–8,AN

Spinal cord
Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping (Svensson, Crawford, & others) 1992;54:74–9*

Spinoplegia
Spinal oxygenation, blood supply localization, cooling, and function with aortic clamping (Svensson, Crawford, & others) 1992;54:74–9*

Stenosis
Competitive flow from a fully patent coronary artery does not limit acute mammary graft flow (Spence, Lust, & others) 1992;54:21–6*

Stents
Expanding wire stents in benign tracheobronchial disease: indications and complications (Nashef, Dromer, & others) 1992;54:937–40*
Management of severe bronchial ischemia after bilateral sequential lung transplantation (Oturanlar, Klepetko, & others) 1992;54:1221–2,CR
Use of endotracheal silicone stents for relief of tracheobronchial obstruction (Gaer, Tsang, & others) 1992;54:512–6*

Sternotomy
Bilateral anterior thoracotomy for automatic implantable cardioverter defibrillator placement in patients with previous sternotomy (Karwande & Rowles) 1992;54:791–3,HW
Limited vertical skin incision for median sternotomy (Tatebe, Eguchi, & others) 1992;54:787–8,HW
Partial median sternotomy for repair of heart defects: a cosmetic approach (Wilson, Ilbawi, & others) 1992;54:892–3*
Prolonged open sternotomy and delayed sternal closure after cardiac operations (Furnary, Magovern, & others) 1992;54:233–9*
Reactive hyperemia in the nonused internal mammary artery after median sternotomy (van Son, Skotnicki, & others) 1992;54:130–3*

Sternum
Modified retractor to prevent peripheral nerve injury (Ancalmo) 1992;54:1249,CP

Subclavian artery
New surgical technique for type B aortic interruption (Kumar, Prabhakar, & others) 1992;54:797–9,HW
Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation (Tsuchida, Hashimoto, & others) 1992;54:161–3,CR

Superior vena cava syndrome
Chronic fibrosing mediastinitis and superior vena caval obstruction from blastomycosis (Lagerstrom, Mitchell, & others) 1992;54:764–5,CR

Superoxide dismutase
Effect of prostaglandin I_2 and superoxide dismutase on reperfusion injury of warm ischemic lung (Yamashita, Oobo, & others) 1992;54:921–4*
Myocardial protection of neonatal heart by cardioplegic solution with recombinant human superoxide dismutase (Tatebe, Nakazawa, & others) 1992;54:124–9*

Surgery, digestive system
Anastomotic ulcer-induced aortoenteric fistula after esophagogastroplasty (Bégin & Sheiner) 1992;54:564–5,CR
Esophagogastrectomy and the variant left hepatic artery (Hemming, Finley, & others) 1992;54:166–8,HW
Transoral cervical esophagogastrostomy using the EEA stapling device (Ancalmo) 1992;54:186,UP

Surgery, lung
Bronchial stump closure (Hoffman & Frater) 1992;54:399,CP
Concomitant cardiac and pulmonary operation: the role of cardiopulmonary bypass (Ulicny, Schmelzer, & others) 1992;54:289–95*
Current morbidity, mortality, and survival after bronchoplastic procedures for malignancy (Tedder, Anstadt, & others) 1992;54:387–91,CV
Imaged thoracic lobectomy: should it be done? (Lewis, Sisler, & Caccavale) 1992;54:80–3*
Lobectomy without a rib spreader (McKneally) 1992;54:2,ED
Long-term survival after resection of pulmonary metastases from carcinoma of the breast (Lanza, Natarajan, & others) 1992;54:244–8*
Pulmonary torsion: a questionnaire survey and a survey of the literature (Wong & Goldstraw) 1992;54:286–8*
Renal cell carcinoma: resection of solitary and multiple metastases (Pogrebniak, Haas, & others) 1992;54:33–8*
Thallium imaging in preoperative evaluation of the pulmonary resection candidate (Miller) 1992;54:249–52*
Thoracoscopic resection of 85 pulmonary lesions (Landreneau, Hazelrigg, & others) 1992;54:415–20*
Treatment of AIDS-related bronchopleural fistula by pleurectomy (Crawford, Galloway, & others) 1992;54:212–5*
Videothoracoscopic wedge excision of the lung (Miller, Allen, & others) 1992;54:410–4*

Surgical flaps
Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR

Surgical staplers
Bronchial stump closure (Hoffman & Frater) 1992;54:399,CP
Manual versus stapled bronchial closure: still controversial (Aguilo & Llobera) 1992;54:1021; Reply (Faber, Vester, & others) 1992;54:1021–2,CP
Temporary double exclusion of the perforated esophagus using absorbable staples (Bardini, Bonavina, & others) 1992;54:1165–7*
Transoral cervical esophagogastrostomy using the EEA stapling device (Ancalmo) 1992;54:186,UP

Suture techniques
Bronchial stump closure (Hoffman & Frater) 1992;54:399,CP

Tachycardia
Accessory atrioventricular node and bundle: a cause of antidromic reentry tachycardia (Sealy, Kopelman, & Murphy) 1992;54:306–10*
Does a posterior aneurysm increase the risk of endocardial resection? (Kron, Kern, & others) 1992;54:617–20*
Late results of operation for ventricular tachycardia (Mickleborough, Mizuno, & others) 1992;54:832–9*
Surgical treatment for ectopic atrial tachycardia (Graffigna, Vigano, & others) 1992;54:338–43*

Takayasu syndrome
Surgical reconstruction of an ascending aortic dissection in Takayasu's arteritis (Haga, Yoshizu, & others) 1992;54:359–60,CR
Teratoma
Exocrine pancreatic function in mediastinal teratomata: an aid to preoperative diagnosis? (Kallis, Treasure, & others) 1992;54:741–3*
Tetralogy of Fallot
Tetralogy of Fallot: favorable outcome of nonneonatal transatrial, transpulmonary repair (Karl, Sano, & others) 1992; 54:903–7*
Thallium
Thallium imaging in preoperative evaluation of the pulmonary resection candidate (Miller) 1992;54:249–52*
Theobromine
Hemolysis after open heart operations (Golino, Stassano, & Spampinato) 1992;54:1246–7,CP; Reply (Okita & Miki) 1992;54:1247,CP
Thermodilution
Comparison of cardiac output measured by intrapulmonary artery Doppler, thermodilution, and electromagnetometry (Heerdt, Pond, & others) 1992;54:959–66*
Thiopental
Barbiturates impair cerebral metabolism during hypothermic circulatory arrest (Siegman, Anderson, & others) 1992;54: 1131–6*
Thoracic arteries
Considerations in the skeletonization technique of internal thoracic artery dissection (Cunningham, Gharavi, & others) 1992;54:947–51*
Preoperative morphologic and physiologic assessment of internal thoracic arteries (Canver) 1992;54:1020–1,CP; Reply (Grover) 1992;54:1021,CP
Thoracic diseases
Present role of thoracoscopy in the diagnosis and treatment of diseases of the chest (Mack, Aronoff, & others) 1992;54: 403–9*
Thoracic injuries
Surgical stabilization of the flail chest (Borioni, Ciani, & others) 1992;54:397–8,CP; Reply (Landreneau) 1992;54:398,CP
Thoracic neoplasms
Intercostal hemangioma presenting as a chest wall tumor (Winchester, Victor, & Fry) 1992;54:145–6,CR
Primary bony and cartilaginous sarcomas of chest wall: results of therapy (Burt, Fulton, & others) 1992;54:226–32*
Thoracic surgery
Imaged thoracic lobectomy: should it be done? (Lewis, Sisler, & Caccavale) 1992;54:80–3*
Lobectomy without a rib spreader (McKneally) 1992;54:2,ED
One hundred consecutive patients undergoing video-assisted thoracic operations (Lewis, Caccavale, & others) 1992;54: 421–6*
Perfusion of dominant left subclavian artery during thoracic aortic aneurysm operation (Tsuchida, Hashimoto, & others) 1992;54:161–3,CR
Pulmonary torsion: a questionnaire survey and a survey of the literature (Wong & Goldstraw) 1992;54:286–8*
Resectional management of thyroid carcinoma invading the airway (Grillo, Suen, & others) 1992;54:3–10*
Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
Surgical stabilization of the flail chest (Borioni, Ciani, & others) 1992;54:397–8,CP; Reply (Landreneau) 1992;54:398,CP
Video-assisted thoracic surgery: basic technical concepts and intercostal approach strategies (Landreneau, Mack, & others) 1992;54:800–7,CV
Thoracic Surgery Foundation for Research and Education
Thoracic Surgery Foundation for Research and Education (Liddle) 1992;54:595,AN
Thoracoscopy
Lobectomy without a rib spreader (McKneally) 1992;54:2,ED
Present role of thoracoscopy in the diagnosis and treatment of diseases of the chest (Mack, Aronoff, & others) 1992;54: 403–9*
Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
Thoracoscopic lung biopsy (McKeown, Conant, & Hubbell) 1992;54:490–2*
Thoracoscopic resection of 85 pulmonary lesions (Landreneau, Hazelrigg, & others) 1992;54:415–20*
Thoracoscopic resection of an anterior mediastinal tumor (Landreneau, Dowling, & others) 1992;54:142–4,CR
Videothoracoscopic enucleation of esophageal leiomyoma (Bardini, Segalin, & others) 1992;54:576–7,HW
Videothoracoscopic wedge excision of the lung (Miller, Allen, & others) 1992;54:410–4*
Thoracotomy
Bilateral anterior thoracotomy for automatic implantable cardioverter defibrillator placement in patients with previous sternotomy (Karwande & Rowles) 1992;54:791–3,HW
Closure of fenestra in Clagett procedure: use of rectus abdominis musculocutaneous flap (Asamura, Goya, & others) 1992;54:147–9,CR
Long-term survival after resection of pulmonary metastases from carcinoma of the breast (Lanza, Natarajan, & others) 1992;54:244–8*
Simplified muscle-sparing thoracotomy for patent ductus arteriosus ligation in neonates (Karwande & Rowles) 1992;54: 164–5,HW
Thrombocytopenia
Aprotinin treatment during open heart operation in a patient with severe thrombocytopenia (Deviri, Izhar, & others) 1992;54:1018–9,CP
Thromboelastography
Thromboelastogram and postoperative hemorrhage (Spiess) 1992;54:810–1,CP (Tuman, McCarthy, & Ivankovich) 1992; 54:811–2,CP; (Martin, Horkay, & others) 1992;54:812–3,CP; Reply (Lin & Wang) 1992;54:813,CP
Thrombolytic therapy
High-dose aprotinin in emergency coronary artery bypass after thrombolysis (Alajmo & Calamai) 1992;54:1022,CP; Reply (Efstratiadis, Munsch, & others) 1992;54:1022–3,CP
Thymoma
Adjuvant radiotherapy after complete resection of thymoma (Haniuda, Morimoto, & others) 1992;54:311–5*
Thoracoscopic resection of an anterior mediastinal tumor (Landreneau, Dowling, & others) 1992;54:142–4,CR
Thyroid neoplasms
Resectional management of thyroid carcinoma invading the airway (Grillo, Suen, & others) 1992;54:3–10*
Tissue adhesives
Surgery of aortic dissections with GRF glue (Zeplin) 1992;54: 1248–9,CP
Tomography, computed
Prognostic significance of computed tomography in resected N2 lung cancer (Cybulsky, Lanza, & others) 1992;54:533–7*

Torsion
Pulmonary torsion: a questionnaire survey and a survey of the literature (Wong & Goldstraw) 1992;54:286–8*

Trachea
Expanding wire stents in benign tracheobronchial disease: indications and complications (Nashef, Dromer, & others) 1992;54:937–40*
Pericardial repair of a tracheal laceration during transhiatal esophagectomy (Gorenstein, Abel, & Patterson) 1992;54:784–6,CR
Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Ricketts) 1992;54:177–83,CT

Tracheal neoplasms
Effect of light dose on the photodynamic destruction of endobronchial tumors (McCaughan, Hawley, & others) 1992;54:705–11*

Tracheal stenosis
Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy (Ziemer, Heinemann, & others) 1992;54:971–3,CR

Tracheoesophageal fistula
Tracheoesophageal fistula after chemotherapy for lymphoma (Sharpe, Sendegeya, & others) 1992;54:366–7,CR

Tracheostomy
Anterior mediastinal tracheostomy with and without cervical exenteration (Orringer) 1992;54:628–37*

Transplantation
Allogenic vein as a conduit for coronary artery bypass (Barner) 1992;54:817,ED
Attenuation of waiting time mortality with heterotopoic heart transplantation (Sekela, Smart, & others) 1992;54:547–51*
Cryopreserved allograft veins as alternative coronary artery bypass conduits: early phase results (Laub, Muralidharan, & others) 1992;54:826–31*
Early cellular events in the lung allograft (Adoumie, Serrick, & others) 1992;54:1071–7*
Heterotopic transplantation: is it a viable alternative? (Baumgartner) 1992;54:401–2,ED
Homograft root replacement for juvenile rheumatoid aortic valve incompetence (Schoof, van Suylen, & Bos) 1992;54:602,CP; Reply (Keeley) 1992;54:602–3,CP
Magnetic resonance imaging evaluation of recipient for cryopreserved aortic allograft (Kon, Link, & others) 1992;54:39–43*
Ross' first homograft replacement of the aortic valve (Gunning) 1992;54:809,CP; Reply (Hopkins) 1992;54:809–10,CP; Reply (Ross) 1992;54:810,CP

Transposition of great vessels
Palliative arterial repair for transposition, ventricular septal defect, and pulmonary vascular disease (Pridjian, Tacy, & others) 1992;54:355–6,CR
Systemic atrioventricular valve replacement in an infant with corrected transposition of the great arteries (Yoshimura, Yamaguchi, & others) 1992;54:573–5,CR
Total correction of transposition of great arteries with atrioventricular septal defect (Kumar, Prabhakar, & others) 1992;54:989–90,CR

Tricuspid valve
Tricuspid valve obstruction caused by plasmacytoma metastasis (Carrel, Linka, & Turina) 1992;54:352–4,CR

Tricuspid valve stenosis
Modified Fontan procedure for severe Ebstein's malformation with predominant tricuspid stenosis (Leung, Lee, & others) 1992;54:523–7*

Triiodothyronine
Acute severe postischemic myocardial depression reversed by triiodothyronine (Holland, Brown, & Clark) 1992;54:301–5*

Tumor metastasis
Renal cell carcinoma: resection of solitary and multiple metastases (Pogrebniak, Haas, & others) 1992;54:33–8*

Tumor necrosis factor
Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass (Jansen, van Oeveren, & others) 1992;54:744–8*

Ultrasonics
Safe intraaortic balloon pump placement through the ascending aorta using transesophageal ultrasound (Kaplan, Weiman, & others) 1992;54:374–5,HW

Ultrasound therapy
Combined conventional mechanical and ultrasonic debridement for aortic valvular stenosis (Baeza, Majid, & others) 1992;54:62–7*

Update
Chemoradiation therapy and resection for carcinoma of the esophagus: short-term results (Parker) 1992;54:808,UP
Combined superior and right lateral left atriotomy with division of the superior vena cava for exposure of the mitral valve (Barner) 1992;54:594,UP
Fluorocarbons: a potential treatment of cerebral air embolism in open-heart surgery (Menasché, Fleury, & Piwnica) 1992;54:392–3,UP
A method for predicting postoperative lung function and its relation to postoperative complications in patients with lung cancer (Nakahara, Miyoshi, & Nakagawa) 1992;54:1016–7,UP
Transoral cervical esophagogastrostomy using the EEA stapling device (Ancalmo) 1992;54:186,UP

Vascular stenosis
Pulmonary artery sling with tracheal stenosis: primary one-stage repair in infancy (Ziemer, Heinemann, & others) 1992;54:971–3,CR

Vascular surgery
Hyperbaric oxygen: value in management of nonhealing saphenectomy wounds (Horowitz, Portogues, & others) 1992;54:782–3,CR
Inverted Y incision for accurate tailoring of patches and vessels (Hoffman & Frater) 1992;54:1228,HW
Pulmonary artery sling (Pawade, de Leval, & others) 1992;54:967–70*

Vasoactive substances
Release of vasoactive substances during cardiopulmonary bypass (Downing & Edmunds) 1992;54:1236–43,CV

Vena cava, superior
Combined superior and right lateral left atriotomy with division of the superior vena cava for exposure of the mitral valve (Barner) 1992;54:594,UP
Retrograde coronary sinus cardioplegia in the presence of persistent left superior vena cava (Shahian) 1992;54:1214–5,CR

Ventricular fibrillation
Electrical instability during reperfusion (Holman) 1992;54:1245–6,CP

Ventricular outflow obstruction
Damus-Stansel-Kaye procedure: technical modifications (Laks, Gates, & others) 1992;54:169–72,HW
Simplified correction of outflow obstruction after mitral valve replacement (Reed & Iverson) 1992;54:985–6,CR

Video-assisted thoracic surgery
- Imaged thoracic lobectomy: should it be done? (Lewis, Sisler, & Caccavale) 1992;54:80–3*
- Lobectomy without a rib spreader (McKneally) 1992;54:2,ED
- One hundred consecutive patients undergoing video-assisted thoracic operations (Lewis, Caccavale, & others) 1992;54:421–6*
- Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery, 1992;54:1,RE
- Video-assisted thoracic surgery: basic technical concepts and intercostal approach strategies (Landreneau, Mack, & others) 1992;54:800–7,CV
- Videothoracoscopic wedge excision of the lung (Miller, Allen, & others) 1992;54:410–4*

Wolff-Parkinson-White syndrome
- Complete cure after a seemingly unsuccessful operation for Wolff-Parkinson-White syndrome (Rakovec, Brecelj, & Zupan) 1992;54:1203–5,CR
- Surgically created Wolff-Parkinson-White syndrome after Fontan operation (Razzouk, Gow, & others) 1992;54:974–7,CR

Wounds, penetrating
- Penetrating cardiac trauma (Ivatury & Rohman) 1992;54:1247–8,CP; Reply (Knott-Craig) 1992;54:1248,CP

Wounds and injuries
- Rupture of the airways from blunt trauma: treatment of complex injuries (Symbas, Justicz, & Ricketts) 1992;54:177–83,CT

VOLUME 54 JULY–DECEMBER 1992

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons
and the Southern Surgical Association

THE ANNALS OF THORACIC SURGERY

Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association

Editor

Thomas B. Ferguson, MD, St. Louis, MO

Herbert Sloan, MD, Editor 1969–1984
John D. Steele, MD, Editor 1964–1969

Associate Editors

John R. Benfield, MD, Sacramento, CA

Anthony R. C. Dobell, MD, Montreal, Canada

Marvin M. Kirsh, MD, Ann Arbor, MI

Hassan Najafi, MD, Chicago, IL

J. Kent Trinkle, MD, Book Review Editor
University of Texas Health Science Center
7703 Floyd Curl Drive, San Antonio, TX 78284-7841

Editorial Board

Hendrick B. Barner, MD, New Hyde Park, NY
Harvey W. Bender, Jr, MD, Nashville, TN
Ray Chu-Jeng Chiu, MD, PhD, Montreal, Canada
Lawrence H. Cohn, MD, Boston, MA
Jack G. Copeland III, MD, Tucson, AZ
Delos M. Cosgrove III, MD, Cleveland, OH
Timothy J. Gardner, MD, Baltimore, MD
William A. Gay, Jr, MD, Salt Lake City, UT
Robert A. Guyton, MD, Atlanta, GA
Clement A. Hiebert, MD, Windham, ME
Takashi Iwa, MD, Kanazawa, Japan
Robert B. Karp, MD, Chicago, IL
James E. Lowe, MD, Durham, NC
Douglas J. Mathisen, MD, Boston, MA
Philippe Menasché, MD, PhD, Paris, France
William I. Norwood, Jr, MD, Philadelphia, PA
John L. Ochsner, MD, New Orleans, LA
Mark B. Orringer, MD, Ann Arbor, MI
Peter C. Pairolero, MD, Rochester, MN
Richard M. Peters, MD, Palo Alto, CA
W. Gerald Rainer, MD, Denver, CO
Charles L. Roper, MD, St. Louis, MO
Thomas W. Shields, MD, Chicago, IL
Jaroslav Stark, MD, London, England
Larry W. Stephenson, MD, Detroit, MI
Kenneth M. Taylor, MD, London, England

Administrative Editor

Carol L. Blasberg, St. Louis, MO

Editorial Office

The Annals of Thoracic Surgery
3108 Queeny Tower
Barnes Hospital Plaza
St. Louis, MO 63110-1041
(314) 361-6084 FAX: (314) 367-0585

To provide a place for ALL thoracic surgeons to relate experiences which will help other practicing thoracic surgeons give better patient care.
Herbert Sloan, MD

Contents

Number 1 **July 1992**

Report

Statement of the AATS/STS Joint Committee on Thoracoscopy and Video Assisted Thoracic Surgery 1

Editorial

Lobectomy Without a Rib Spreader 2

Martin F. McKneally, MD, PhD

Original Articles

Resectional Management of Thyroid Carcinoma Invading the Airway 3

Hermes C. Grillo, MD, Hon Chi Suen, MBBS, Douglas J. Mathisen, MD, and John C. Wain, MD

Intraaortic Balloon Counterpulsation: Patterns of Usage and Outcome in Cardiac Surgery Patients 11

Lawrence L. Creswell, MD, Michael Rosenbloom, MD, James L. Cox, MD, Thomas B. Ferguson, Sr, MD, Nicholas T. Kouchoukos, MD, Thomas L. Spray, MD, Michael K. Pasque, MD, T. Bruce Ferguson, Jr, MD, Thomas H. Wareing, MD, and Charles B. Huddleston, MD

Competitive Flow From a Fully Patent Coronary Artery Does Not Limit Acute Mammary Graft Flow 21

Paul A. Spence, MD, Robert M. Lust, PhD, Richard S. Zeri, MD, Stanley R. Jolly, PhD, Prabodh M. Mehta, MD, Masaki Otaki, MD, You Su Sun, MD, and W. Randolph Chitwood, Jr, MD

Double-Lung Transplantation for Cystic Fibrosis 27

Hani Shennib, MD, Michel Noirclerc, MD, Pierre Ernst, MD, Dominique Metras, MD, David S. Mulder, MD, Roger Giudicelli, MD, François Lebel, MD, Jean-François Dumon, MD, and the Cystic Fibrosis Transplant Study Group

Renal Cell Carcinoma: Resection of Solitary and Multiple Metastases 33

Helen W. Pogrebniak, MD, Gabe Haas, MD, W. Marston Linehan, MD, Steven A. Rosenberg, MD, PhD, and Harvey I. Pass, MD

Magnetic Resonance Imaging Evaluation of Recipient for Cryopreserved Aortic Allograft 39

Neal D. Kon, MD, Kerry M. Link, MD, William P. Buchanan, MD, Abdel-Mohsen Nomeir, MD, Thomas R. Downes, MD, and A. Robert Cordell, MD

Usefulness of Right Ventricular Indices in Early Diagnosis of Cardiac Tamponade 44

James W. Jones, MD, PhD, Najwa N. Izzat, PhD, Mohamed N. Rashad, MD, John I. Thornby, PhD, Thomas R. McLean, MD, Lars G. Svensson, MD, PhD, and Arthur C. Beall, Jr, MD

Bronchial Carcinoid Tumors: A Retrospective Analysis of 126 Patients 50

David H. Harpole, Jr, MD, Jerome M. Feldman, MD, Scott Buchanan, MD, W. Glenn Young, MD, and Walter G. Wolfe, MD

Retrograde Versus Antegrade Cardioplegia: Impact on Right Ventricular Function 56

E. Charles Douville, MD, John M. Kratz, MD, Francis G. Spinale, PhD, Fred A. Crawford, Jr, MD, Calvert C. Alpert, MD, and Andrew Pearce, BS

Combined Conventional Mechanical and Ultrasonic Debridement for Aortic Valvular Stenosis 62

Oscar R. Baeza, MD, Naweed K. Majid, MD, Daniel P. Conroy, MD, and James S. Donahoo, MD

Mitral Valve Replacement: Randomized Trial of St. Jude and Medtronic-Hall Prostheses 68

Andrew C. Fiore, MD, Keith S. Naunheim, MD, Stephen D'Orazio, MD, George C. Kaiser, MD, Lawrence R. McBride, MD, D. Glenn Pennington, MD, Pamela S. Peigh, MD, Vallee L. Willman, MD, Arthur J. Labovitz, MD, and Hendrick B. Barner, MD

Spinal Oxygenation, Blood Supply Localization, Cooling, and Function With Aortic Clamping 74

Lars G. Svensson, MD, E. Stanley Crawford, MD, Vasishta Patel, MD, Thomas R. McLean, MD, James W. Jones, MD, and Michael E. DeBakey, MD

Imaged Thoracic Lobectomy: Should It Be Done? 80

Ralph J. Lewis, MD, Glenn E. Sisler, MD, and Robert J. Caccavale, MD

Elective Pneumonectomy: Factors Associated With Morbidity and Operative Mortality 84

Ramesh L. Patel, FRCS(Ed), Edward R. Townsend, FRCS, and S. William Fountain, FRCS

Mitral Valve Repair in Patients With Endomyocardial Fibrosis 89

Miguel Sousa Uva, MD, Victor A. Jebara, MD, Christophe Acar, MD, Patrice Dervanian, MD, Sylvain Chauvaud, MD, Jean F. Fuzellier, MD, Jean-Noël Fabiani, MD, Alain Deloche, MD, and Alain F. Carpentier, MD, PhD

Acadesine (AICA-riboside) Improves Postischemic Cardiac Recovery 93

Steven F. Bolling, MD, Mark A. Groh, MD, Ann M. Mattson, BA, Russell A. Grinage, and Kim P. Gallagher, PhD

Primary Lung Cancer in Young Patients: A Study of 82 Surgically Treated Patients 99

Philippe Icard, MD, Jean-François Regnard, MD, Stéphan de Napoli, MD, Antonio Rojas-Miranda, MD, Philippe Dartevelle, MD, and Philippe Levasseur, MD

Production and Reversibility of Right Ventricular Hypertrophy and Right Heart Failure in Dogs 104

Chia-Ming Hsieh, MD, Gregory J. Mishkel, MD, Paulo F. G. Cardoso, MD, Harry Rakowski, MD, Stephen C. Dunn, MD, Jagdish Butany, MD, Richard D. Weisel, MD, G. Alexander Patterson, MD, and Joel D. Cooper, MD

Ionescu-Shiley Valve Failure I: Experience With 125 Standard-Profile Explants 111

Virginia M. Walley, MD, Claudia A. Keon, BSc, Mandana Khalili, David Moher, MSc, Martine Campagna, RT, and Wilbert J. Keon, MD

Ionescu-Shiley Valve Failure II: Experience With 25 Low-Profile Explants 117

Virginia M. Walley, MD, Claudia A. Keon, BSc, Mandana Khalili, David Moher, MSc, Martine Campagna, RT, and Wilbert J. Keon, MD

Myocardial Protection of Neonatal Heart by Cardioplegic Solution With Recombinant Human Superoxide Dismutase 124

Shoh Tatebe, MD, Mikio Nakazawa, PhD, Haruo Miyamura, MD, Jun-ichi Hayashi, MD, Shoji Eguchi, MD, and Shoichi Imai, MD

Reactive Hyperemia in the Nonused Internal Mammary Artery After Median Sternotomy 130

Jacques A. M. van Son, MD, PhD, Stefan H. Skotnicki, MD, Heino A. Folmer, MD, and Wim N. J. C. van Asten, PhD

Surgical Implications of Juxtaposed Atrial Appendages and the Associated Anomalies 134

Min-Reu Leu, MD, Ing-Sh Chiu, MD, PhD, Chi-Ren Hung, MD, and Mei-Hwan Wu, MD

Coarctation Repair in Neonates With Subclavian-Sparing Advancement Flap 137

Baljit K. Sharma, MD, Moises Calderon, MD, and David A. Ott, MD

Case Reports

Thoracoscopic Resection of an Anterior Mediastinal Tumor 142

Rodney J. Landreneau, MD, Robert D. Dowling, MD, William M. Castillo, MD, and Peter F. Ferson, MD

Intercostal Hemangioma Presenting as a Chest Wall Tumor 145

David J. Winchester, MD, Thomas A. Victor, MD, PhD, and Willard A. Fry, MD

Closure of Fenestra in Clagett Procedure: Use of Rectus Abdominis Musculocutaneous Flap 147

Hisao Asamura, MD, Tomoyuki Goya, MS, Tsuguo Naruke, MD, Ryosuke Tsuchiya, MD, Haruhiko Kondo, MD, Keiichi Suemasu, MD, and Takashi Nakatsuka, MD

Carbon Dioxide Prevents Pulmonary Overcirculation in Hypoplastic Left Heart Syndrome 150

David R. Jobes, MD, Susan C. Nicolson, MD, James M. Steven, MD, Margaret Miller, MD, Marshall L. Jacobs, MD, and William I. Norwood, Jr, MD, PhD

Early Structural Deterioration With the Mitroflow Pericardial Xenograft in the Mitral Position 152

Jose M. Bernal, MD, Jose M. Rabasa, MD, Jose R. Echevarria, MD, and Jose M. Revuelta, MD

Aortoesophageal Fistula Induced by Foreign Bodies 155

Ming-Ho Wu, MD, and Wu-Wei Lai, MD

Combined Traumatic Avulsion of the Aortic Valve and Rupture of the Left Common Carotid Artery 157

L. W. Ernest van Heurn, MD, Ruben P. H. M. Hamerlijnck, MD, Aart Brutel de la Rivière, MD, Maarten J. Suttorp, MD, Sjef M. P. G. Ernst, MD, and Freddy E. E. Vermeulen, MD

Central Cyanosis Due to Prominence of the Eustachian and Thebesian Valves 159

Hassan Raffa, FRCS(G), Khalid Al-Ibrahim, FRCS(C), Mohamed Taher Kayali, FRCS(G), Abdool Aniff Sorefan, FRCS(Eng), and Majd Rustom, MD, CES

Perfusion of Dominant Left Subclavian Artery During Thoracic Aortic Aneurysm Operation 161

Koki Tsuchida, MD, Akimasa Hashimoto, MD, Masahiro Endo, MD, and Hitoshi Koyanagi, MD

How to Do It

Simplified Muscle-Sparing Thoracotomy for Patent Ductus Arteriosus Ligation in Neonates 164

Shreekanth V. Karwande, MD, and John R. Rowles, MD

Esophagogastrectomy and the Variant Left Hepatic Artery 166

Alan W. Hemming, MD, Richard J. Finley, MD, Kenneth G. Evans, MD, Bill Nelems, MD, and Guy Fradet, MD

Damus-Stansel-Kaye Procedure: Technical Modifications 169

Hillel Laks, MD, Richard N. Gates, MD, Amir Elami, MD, and Jeffrey M. Pearl, MD

Subfascial Implantation of Implantable Cardioverter Defibrillator Generator 173

David M. Shahian, MD, Warren A. Williamson, MD, John M. Streitz, Jr, MD, and Ferdinand J. Venditti, MD

Mechanical Support for Intraventricular Decompression in Repair of Left Ventricular Disruption 175

Robert T. Baldwin, MD, and Denton A. Cooley, MD

Collective Review

Rupture of the Airways From Blunt Trauma: Treatment of Complex Injuries 177

Panagiotis N. Symbas, MD, Alexander G. Justicz, MD, and Richard R. Ricketts, MD

Key References

Physician Payment Reform: A Bibliography 184

George E. Miller, Jr, MD

Update

Transoral Cervical Esophagogastrostomy Using the EEA Stapling Device 186

Nelson Ancalmo, MD

Correspondence

Total Orthotopic Heart Transplantation: An Alternative to the Standard Technique 187

Simon W. H. Kendall, FRCSEd, F. Ciulli, MD, P. A. Mullins, MRCP, B. Biocina, MD, J. J. Dunning, FRCSEd, and Stephen R. Large, FRCS

Reply

Gilles Dreyfus, MD

A New Idea 188

Wilford B. Neptune, MD

Rereplacement of the Mitral Valve With Represervation of the Subvalvular Apparatus 188

Gordon N. Olinger, MD

Modified Technique of Internal Mammary Artery Harvest 190

Srikrishna Sirivella, MD, Isaac Gielchinsky, MD, and Victor Parsonnet, MD

Reply

Lindsay C. H. John, FRCS, S. J. Edmondson, FRCS, and Gareth M. Rees, FRCS

Ischemic Mitral Valve Repair 190

Tsung O. Cheng, MD

Acute Pulmonary Edema in Closed Mitral Commissurotomy 191

Prabhat Tewari, MD, and Monica Kumar, MD

Pericardial Window 191

Dov Weissberg, MD

Reply

Safuh Attar, MD, and Joseph S. McLaughlin, MD

Reply

David H. Spodick, MD

Announcements

Information for Authors A-23, 24

Guidelines for the Submission of Electronic Manuscripts A-25

Events of Interest A-26, 27

Forthcoming Articles A-28

Notice From The Society of Thoracic Surgeons 10, 92

Notice From the Southern Thoracic Surgical Association 98

Notice From the American Board of Thoracic Surgery 103, 116

Classified Advertisements A-31, 32

Call for Abstracts, The Society of Thoracic Surgeons A-33, 34

Information About Membership in The Society of Thoracic Surgeons A-35

Index to Advertisers A-40

Number 2 August 1992

Herbert Sloan Lecture

The International Cardiothoracic Surgeon 193

Mark V. Braimbridge, MA, MB, BChir(Cantab), FRCS(Eng)

Original Articles

Barrett's Esophagus With High-Grade Dysplasia: An Indication for Esophagectomy? 199

Manuel Pera, MD, Victor F. Trastek, MD, Herschel A. Carpenter, MD, Mark S. Allen, MD, Claude Deschamps, MD, and Peter C. Pairolero, MD

Clinical Trial of FK 506 Immunosuppression in Adult Cardiac Transplantation 205

John M. Armitage, MD, Robert L. Kormos, MD, Shigeki Morita, MD, John Fung, MD, Gary C. Marrone, MD, Robert L. Hardesty, MD, Bartley P. Griffith, MD, and Thomas E. Starzl, MD, PhD

Treatment of AIDS-Related Bronchopleural Fistula by Pleurectomy 212

Bernard K. Crawford, MD, Aubrey C. Galloway, MD, Arthur D. Boyd, MD, and Frank C. Spencer, MD

Pediatric Lung Transplantation for Pulmonary Hypertension and Congenital Heart Disease 216

Thomas L. Spray, MD, George B. Mallory, MD, Charles E. Canter, MD, Charles B. Huddleston, MD, and Larry R. Kaiser, MD

Primary Bony and Cartilaginous Sarcomas of Chest Wall: Results of Therapy 226

Michael Burt, MD, PhD, Michael Fulton, BS, Susan Wessner-Dunlap, MD, Martin Karpeh, MD, Andrew G. Huvos, MD, Manjit S. Bains, MD, Nael Martini, MD, Patricia M. McCormack, MD, Valerie W. Rusch, MD, and Robert J. Ginsberg, MD

Prolonged Open Sternotomy and Delayed Sternal Closure After Cardiac Operations 233

Anthony P. Furnary, MD, James A. Magovern, MD, Kathleen A. Simpson, BS, and George J. Magovern, MD

A Staged Expanding Pulmonary Artery Band 240

E. Taliaferro Warren, MD, Bobby J. Heath, MD, and Woodrow W. Brand III, MD

Long-Term Survival After Resection of Pulmonary Metastases From Carcinoma of the Breast 244

Louis A. Lanza, MD, Giri Natarajan, MA, Jack A. Roth, MD, and Joe B. Putnam, Jr, MD

Thallium Imaging in Preoperative Evaluation of the Pulmonary Resection Candidate 249

Joseph I. Miller, Jr, MD

Hypothermic Thoracic and Thoracoabdominal Aneurysm Operation: A Central Cannulation Technique 253

Stephen Westaby, FRCS

Glucose and Insulin Supply Before Cardiopulmonary Bypass in Cardiac Surgery: A Double-Blind Study 259

Claude Girard, MD, Pierre Quentin, MD, Hélène Bouvier, MD, Pascale Blanc, MD, Olivier Bastien, MD, Jean-Jacques Lehot, MD, Philippe Mikaeloff, MD, and Suzanne Estanove, MD

Morphology of the Posterior Junctional Area in Atrioventricular Septal Defects 264

Siew Yen Ho, PhD, Leon M. Gerlis, FRCPath, Julie Toms, Christopher Lincoln, MBBS, and Robert H. Anderson, MD

Long-Term Follow-up Results After Reconstruction of the Mitral Valve by Leaflet Advancement 271

Kouichi Hisatomi, MD, Tadashi Isomura, MD, Akio Hirano, MD, Tohru Sato, MD, Masaru Nishimi, MD, Takemi Kawara, MD, and Kiroku Ohishi, MD

Successful Treatment of Postoperative Chylothorax Using an External Pleuroperitoneal Shunt 276

Steven P. Cummings, MD, David A. Wyatt, MD, Joseph W. Baker, MD, Terry L. Flanagan, MPH, William D. Spotnitz, MD, Bradley M. Rodgers, MD, Irving L. Kron, MD, and Curtis G. Tribble, MD

Thoracic Aortic Operations in Patients Aged 70 Years or Older 279

Koichi Tabayashi, MD, Mikio Ohmi, MD, Yoshimi Syohji, MD, Hiroji Akimoto, MD, Katuo Matuki, MD, Yuusuke Turu, MD, and Hitoshi Mohri, MD

Long-Term Results of the Ivalon Baffle Mitral Valve Repair 283

John A. Odell, FRCS(Ed), Joseph O. Schurek, Christiaan N. Barnard, MD, PhD, and Patrick J. Commerford, FCP(SA)

Pulmonary Torsion: A Questionnaire Survey and a Survey of the Literature 286

Poo Sing Wong, FRCS, and Peter Goldstraw, FRCS

Concomitant Cardiac and Pulmonary Operation: The Role of Cardiopulmonary Bypass 289

Karl S. Ulicny, Jr, MD, Victor Schmelzer, MD, John B. Flege, Jr, MD, Joseph C. Todd, MD, Donald L. Mitts, MD, David B. Melvin, MD, and Creighton B. Wright, MD

Open Lung Biopsy for Diffuse Infiltrative Lung Disease 296

Vijay Chechani, MD, Rodney J. Landreneau, MD, and Shabbir S. Shaikh, MD

Acute Severe Postischemic Myocardial Depression Reversed by Triiodothyronine 301

Fred W. Holland II, MD, Paul S. Brown, Jr, MD, and Richard E. Clark, MD

Accessory Atrioventricular Node and Bundle: A Cause of Antidromic Reentry Tachycardia 306

Will C. Sealy, MD, Harry E. Kopelman, MD, and Douglas A. Murphy, MD

Adjuvant Radiotherapy After Complete Resection of Thymoma 311

Masayuki Haniuda, MD, Masami Morimoto, MD, Hideki Nishimura, MD,
Osamu Kobayashi, MD, Takeshi Yamanda, MD, and Futoshi Iida, MD

Skeletal Muscle Ventricles as Left Atrial–Aortic Pumps: Short-Term Studies 316

Timothy L. Hooper, MD, Hiroshi Niinami, MD, Robert L. Hammond, BA,
Huiping Lu, MD, Renato Ruggiero, MD, Alberto Pochettino, MD, and
Larry W. Stephenson, MD

Isolated Extracardiac Unruptured Sinus of Valsalva Aneurysms 323

Victor A. Jebara, MD, Sylvain Chauvaud, MD, Michele Portoghese, MD,
Miguel Sousa Uva, MD, Christophe Acar, MD, Arnaud Farge, MD,
Patrice Dervanian, MD, Antoine Sarkis, MD, Patrick Bruneval, MD,
Jean-Noël Fabiani, MD, Alain Deloche, MD, and Alain F. Carpentier, MD, PhD

A Prostacyclin Analogue Reduces Free Radical Generation in Heart-Lung Transplantation 327

Koh Takeuchi, MD, Sohei Suzuki, MD, Norio Kako, MD, Makoto Kobayashi, MD,
Shoichi Takahashi, MD, Mitsuhiro Sawada, MD, Takemi Honma, MD,
Satoshi Iwabuchi, MD, Kozo Fukui, MD, Koichi Koyama, MD, and Hisaaki Koie, MD

Heterotopic Heart Transplantation and Recipient Heart Operation in Ischemic Heart Disease 333

Paul D. Ridley, FRCS, Asghar Khaghani, FRCS, Francesco Musumeci, MD,
Roberto Favaloro, MD, El-Sayed Akl, MD, Nick R. Banner, MRCP,
Andrew G. Mitchell, MRCP, and Magdi H. Yacoub, FRCS

Surgical Treatment for Ectopic Atrial Tachycardia 338

Angelo Graffigna, MD, Mario Vigano, MD, Francesco Pagani, MD, and
Giorgio Salerno, MD

Univentricular Atrioventricular Connection With Subaortic Stenosis: A Staged Surgical Approach 344

Steven A. Webber, MB, ChB, Suvro S. Sett, MD, and Jacques G. LeBlanc, MD

Optimal Level of Hypothermia for Prolonged Myocardial Protection Assessed by ^{31}P Nuclear Magnetic Resonance 348

Matthias Karck, MD, Antonio Vivi, MSc, Maria Tassini, MSc, Herzl Schwalb, PhD,
Nadir Askenasy, MD, Hadar Merchav, MD, Gil Navon, PhD, and Gideon Uretzky, MD

Case Reports

Tricuspid Valve Obstruction Caused by Plasmacytoma Metastasis 352

Thierry Carrel, MD, André Linka, MD, and Marko I. Turina, MD

Palliative Arterial Repair for Transposition, Ventricular Septal Defect, and Pulmonary Vascular Disease 355

Ara K. Pridjian, MD, Theresa A. Tacy, MD, Douglas Teske, MD, and
Edward L. Bove, MD

Bilateral Adrenal Hemorrhage After an Open Heart Operation 357

Windsor Ting, MD, John L. Nosher, MD, Peter M. Scholz, MD, and Alan J. Spotnitz, MD

Surgical Reconstruction of an Ascending Aortic Dissection in Takayasu's Arteritis 359

Yoshiyuki Haga, MD, Hiroshi Yoshizu, MD, Eriya Okuda, MD, Yozo Uriuda, MD, Atsuhiro Mitsumaru, MD, Seiichi Tamai, MD, and Susumu Tanaka, MD

Cardiopulmonary Bypass in the Early Puerperium: Possible New Role for Aprotinin 361

Mauro Lamarra, MD, Ahmed A. Azzu, FRCS, and E. Nihal P. Kulatilake, FRCS

Combined Maze Procedure and Septal Myectomy in a Septuagenarian 364

Arie Blitz, MD, David McLoughlin, MD, Jay Gross, MD, Daniel S. Schwartz, MD, John D. Fisher, MD, Soo G. Kim, MD, Rosemary Frame, RN, and Richard F. Brodman, MD

Tracheoesophageal Fistula After Chemotherapy for Lymphoma 366

D. A. C. Sharpe, FRCS, S. Z. Sendegeya, FRCS, D. H. Parry, FRCPath, and M. J. Drakeley, FRCS

Congenital Aortic Stenosis and Patent Ductus Arteriosus in the Adult 368

Donald D. Glower, MD, Thomas M. Bashore, MD, and Charles E. Spritzer, MD

Extracardiac Total Cavopulmonary Connection 371

John C. Laschinger, MD, Richard E. Ringel, MD, Joel I. Brenner, MD, and Joseph S. McLaughlin, MD

How to Do It

Safe Intraaortic Balloon Pump Placement Through the Ascending Aorta Using Transesophageal Ultrasound 374

Lewis J. Kaplan, MD, Darryl S. Weiman, MD, Nicholas Langan, MD, Alexis B. Sokil, MD, and Glenn J. R. Whitman, MD

Approach for Insertion of Aortic Composite Valve Grafts 376

Lars G. Svensson, MD, PhD

Method of Single-Lung Transplantation in the Absence of a Left Atrial Cuff 379

Graeme L. Hammond, MD, Kenneth L. Franco, MD, and John C. Baldwin, MD

Right Internal Mammary Artery Extended With an Inferior Epigastric Artery for Circumflex and Right Coronary Bypass 381

Michel Buche, MD, Erwin Schroeder, MD, Philippe Devaux, MD, Yves A. G. Louagie, MD, and Jean-Claude Schoevaerdts, MD

Cervical Esophago-esophageal Anastomosis 384

Charles D. Fraser, MD, and Richard F. Heitmiller, MD

Current Review

Current Morbidity, Mortality, and Survival After Bronchoplastic Procedures for Malignancy 387

Mark Tedder, MD, Mark P. Anstadt, MD, Stephen D. Tedder, BS, and
James E. Lowe, MD

Update

Fluorocarbons: A Potential Treatment of Cerebral Air Embolism in Open-Heart Surgery 392

Philippe Menasché, MD, PhD, Jean-Pierre Fleury, MD, and Armand Piwnica, MD

Correspondence

Retrograde Disc Escape in a Harken Mitral Valve Prosthesis 394

Robert L. Berger, MD

Reply

Eduardo Otero-Coto, MD, PhD

Coronary Bypass Graft Aneurysm 395

Wadih R. Dimitri, FRCS, and Allan W. Reid, FRCR

Role of the Bronchial Arteries in Lung Function 395

Rogelio A. Ventemiglia, MD

Reply

Hans H. J. Schreinemakers, MD, Paul R. J. De Leyn, MD, Marco Marcus, MD,
Patrick Wouters, MD, Philippe L. E. Moerman, MD, Willem Flameng, MD,
Tony Lerut, MD, and Joel D. Cooper, MD

Reply

Louis Couraud, MD, Eugène M. Baudet, MD, Christian Martigne, MD,
Xavier F. Roques, MD, Jean-François Velly, MD, Nadine Laborde, MD, Jean Dubrez, MD,
Fréderic Clerc, MD, Claire Dromer, MD, and Eric Vallieres, MD

Surgical Stabilization of the Flail Chest 397

Raoul Borioni, MD, Renzo Ciani, MD, Guglielmo M. Actis Dato, MD, and
Raffaele Garofalo, MD

Reply

Rodney J. Landreneau, MD

Bronchial Stump Closure 399

Darryl Hoffman, FRCS, and Robert W. M. Frater, MD

Better Salvage in Non–Small Cell Lung Cancer 399

John S. Chambers, MD

Announcements

Information for Authors A-23, 24

Guidelines for the Submission of Electronic Manuscripts A-25

Events of Interest A-27, 28

Forthcoming Articles A-30

Notice From The Society of Thoracic Surgeons 248, 315

Notice From the American Board of Thoracic Surgery 354, 383

Classified Advertisements A-31, 32, 33

Information About Membership in The Society of Thoracic Surgeons A-34

Call for Abstracts, The Society of Thoracic Surgeons A-35, 36

Index to Advertisers A-40

Number 3 September 1992

Editorial

Heterotopic Transplantation: Is It a Viable Alternative? 401

William A. Baumgartner, MD

Original Articles

Present Role of Thoracoscopy in the Diagnosis and Treatment of Diseases of the Chest 403

Michael J. Mack, MD, Ronald J. Aronoff, MD, Tea E. Acuff, MD, Mark B. Douthit, MD, Richard T. Bowman, MD, and William H. Ryan, MD

Videothoracoscopic Wedge Excision of the Lung 410

Daniel L. Miller, MD, Mark S. Allen, MD, Victor F. Trastek, MD, Claude Deschamps, MD, and Peter C. Pairolero, MD

Thoracoscopic Resection of 85 Pulmonary Lesions 415

Rodney J. Landreneau, MD, Stephen R. Hazelrigg, MD, Peter F. Ferson, MD, Joel A. Johnson, MD, Weerchai Nawarawong, MD, Theresa M. Boley, RN, MSN, Jack J. Curtis, MD, Claudia M. Bowers, RN, David B. Herlan, MD, and Robert D. Dowling, MD

One Hundred Consecutive Patients Undergoing Video-Assisted Thoracic Operations 421

Ralph J. Lewis, MD, Robert J. Caccavale, MD, Glenn E. Sisler, MD, and James W. Mackenzie, MD

Composite Valve Graft Replacement of the Proximal Aorta: Comparison of Techniques in 348 Patients 427

Lars G. Svensson, MD, PhD, E. Stanley Crawford, MD, Kenneth R. Hess, MS, Joseph S. Coselli, MD, and Hazim J. Safi, MD

Factors Affecting Mitral Valve Reoperation in 317 Survivors After Mitral Valve Reconstruction 440

Javier Fernandez, MD, Douglas H. Joyce, DO, Kathryn Hirschfeld, RN, Chao Chen, PhD, Glenn W. Laub, MD, Mark S. Adkins, MD, William A. Anderson, MD, James W. Mackenzie, MD, and Lynn B. McGrath, MD

A Randomized Study of the Systemic Effects of Warm Heart Surgery 449

George T. Christakis, MD, Jean Paul Koch, MD, Kathy A. Deemar, CCP, Stephen E. Fremes, MD, Lesley Sinclair, MD, Erluo Chen, MPH, Tomas A. Salerno, MD, Bernard S. Goldman, MD, and Samuel V. Lichtenstein, MD, PhD

Survival After Resection of Stage II Non–Small Cell Lung Cancer 460

Nael Martini, MD, Michael E. Burt, MD, PhD, Manjit S. Bains, MD, Patricia M. McCormack, MD, Valerie W. Rusch, MD, and Robert J. Ginsberg, MD

Optimum Treatment of Discrete Subaortic Stenosis 467

Flavian M. Lupinetti, MD, Ara K. Pridjian, MD, Louise B. Callow, RN, Dennis C. Crowley, MD, Robert H. Beekman, MD, and Edward L. Bove, MD

Normothermic Cardioplegia: Is Aortic Cross-Clamping Still Synonymous With Myocardial Ischemia? 472

Philippe Menasché, MD, PhD, Jacqueline Peynet, MD, Bernard Touchot, MD, Mohamed Aziz, MD, Sam Haydar, MD, Ghislaine Perez, MD, Line Veyssié, MD, Juan Montenegro, MD, Gérard Bloch, MD, and Armand Piwnica, MD

Subcutaneous Use of Erythropoietin in Heart Surgery 479

Yasunori Watanabe, MD, Katsuo Fuse, MD, Yoshihiro Naruse, MD, Toshiya Kobayashi, MD, Shin Yamamoto, MD, Hiroaki Konishi, MD, Taikoh Horii, MD, and Yoichi Shibata, MD

Atrioventricular Pacing in Congenital Heart Disease 485

John M. Kratz, MD, Paul C. Gillette, MD, Fred A. Crawford, MD, Robert M. Sade, MD, and Vicki L. Zeigler, RN

Thoracoscopic Lung Biopsy 490

Peter P. McKeown, FRACS, Patricia Conant, MS, ARNP, and David S. Hubbell, MD

Multimodal Therapy of Small Cell Lung Cancer in TNM Stages I through IIIa 493

Ludwig C. Müller, MD, Georg M. Salzer, MD, Heinz Huber, MD, Christian Prior, MD, Ingrid Ebner, MD, Hermann Frommhold, MD, and Heinz-Wolfgang Präuer, MD

Results of Operation Without Adjuvant Therapy in the Treatment of Small Cell Lung Cancer 498

Samir S. Shah, MBBS, Joao Thompson, MD, and Peter Goldstraw, FRCS

Human Cardiac Nerve Stimulation 502

David A. Murphy, MD, and J. Andrew Armour, MD, PhD

Is Use of the Intraaortic Balloon Pump in Octogenarians Justified? 507

Donato A. Sisto, FACS, Darryl M. Hoffman, FRCS, Sylvia Fernandes, MD, and Robert W. M. Frater, FRCS

Use of Endotracheal Silicone Stents for Relief of Tracheobronchial Obstruction 512

Jullien A. R. Gaer, FRCSEd, Victor Tsang, FRCS, Azghar Khaghani, FRCSEd, C. E. Gillbe, FCAnaes, Edward R. Townsend, FRCS, S. William Fountain, FRCS, and Magdi H. Yacoub, FRCS

Multicenter Trial of Automated Nitroprusside Infusion for Postoperative Hypertension 517

W. Randolph Chitwood, Jr, MD, Delos M. Cosgrove III, MD, Robert M. Lust, PhD, and the Titrator Multicenter Study Group

Modified Fontan Procedure for Severe Ebstein's Malformation With Predominant Tricuspid Stenosis 523

Maurice P. Leung, MBBS, Jan Lee, MBBS, Roxy N. S. Lo, MBBS, and C. K. Mok, MBBS

Experience in 100 Transthoracic Balloon Pumps 528

Stephen R. Hazelrigg, MD, James E. Auer, MD, and Paul E. Seifert, MD

Prognostic Significance of Computed Tomography in Resected N2 Lung Cancer 533

Irene J. Cybulsky, MD, Louis A. Lanza, MD, M. Bernadette Ryan, MD, Joe B. Putnam, Jr, MD, Marion M. McMurtrey, MD, and Jack A. Roth, MD

Long-Term Results of St. Jude Medical Valve in the Tricuspid Position 538

Arun K. Singh, MD, William C. Feng, MD, and Stephen J. Sanofsky, MD

Coagulation Defects in Neonates During Cardiopulmonary Bypass 541

Frank H. Kern, MD, Nicholas J. Morana, BS, John J. Sears, BS, and Paul R. Hickey, MD

Attenuation of Waiting Time Mortality With Heterotopic Heart Transplantation 547

Michael E. Sekela, MD, Frank W. Smart, MD, George P. Noon, MD, and James B. Young, MD

Case Reports

Cardiac Valve Replacement in Patients Infected With the Human Immunodeficiency Virus 552

Norbert Bräu, MD, Rick A. Esposito, MD, and Michael S. Simberkoff, MD

Replacement of the Valvular Prosthesis in a Patient With a Bentall Procedure 555

Anthony L. Panos, MD, Kevin T. Teoh, MD, John K. Wilson, MD, and Tomas A. Salerno, MD

Repair of Aortico–Left Ventricular Tunnel Associated With Subpulmonary Obstruction 557

Christopher J. Knott-Craig, MMed(Thor), Pieter L. van der Merwe, MD, Neale N. Kalis, MMed(Ped), and Joan Hunter, MMed(Ped)

Mediastinal Window: A Cause of Simultaneous Bilateral Spontaneous Pneumothorax 560

Tatu Juvonen, MD, Martti Lepojärvi, MD, Risto Pokela, MD, Jukka Juvonen, MD, and Matti I. Kairaluoma, MD

Intraoperative Echocardiographic Diagnosis of Previously Unrecognized Cor Triatriatum 562

Charles W. Hogue, Jr, MD, Benico Barzilai, MD, Robert Forstot, MD,
Todd S. Shuman, MD, and James L. Cox, MD

Anastomotic Ulcer-Induced Aortoenteric Fistula After Esophagogastroplasty 564

Louis R. Bégin, MD, and Nathan M. Sheiner, MD

Retrograde Cerebral Perfusion With Circulatory Arrest in Aortic Arch Aneurysms 566

Chojiro Yamashita, MD, Hiroomi Nakamura, MD, Yasuyuki Nishikawa, MD,
Sinichiro Yamamoto, MD, Masayoshi Okada, MD, and Kazuo Nakamura, MD

Pericardioperitoneal Shunt for Persistent Pericardial Effusions: A New Drainage Procedure 569

Thomas F. Molnar, MD, and Kumarasingham Jeyasingham, FRCS

Coronary Artery Bypass Grafting Nine Years After Cardiac Transplantation 571

John J. Dunning, FRCSEd, Simon W. H. Kendall, FRCSEd, Paul A. Mullins, MRCP,
Anoop Chauhan, MRCP, Timothy R. Graham, FRCS, Bojin Biocina, MD,
Peter M. Schofield, MRCP, and Stephen R. Large, FRCS

Systemic Atrioventricular Valve Replacement in an Infant With Corrected Transposition of the Great Arteries 573

Naoki Yoshimura, MD, Masahiro Yamaguchi, MD, Yoshihiro Oshima, MD,
Hidetaka Ohashi, MD, Masanao Imai, MD, Hee-Nam Chung, MD, and Eiryu Kyo, MD

How to Do It

Videothoracoscopic Enucleation of Esophageal Leiomyoma 576

Romeo Bardini, MD, Andrea Segalin, MD, Alberto Ruol, MD, Maurizio Pavanello, MD,
and Alberto Peracchia, MD

Placement of an Endotracheal Tube in the Short Tracheal Stump 578

Daniel P. Pellegrini, MD, Samuel J. Mucci, MD, Dennis S. Durzinsky, MD, and
Prabir K. Chaudhuri, MD

Simple Method to Monitor Pulmonary Artery Pressure in Infants After Cardiac Operations 580

Charles A. Dietl, MD, and Alberto R. Torres, MD

Management of Aortic Cannulation Site Blowouts 582

Szabolcs Szentpetery, MD

Pericardioplasty 584

Carlos A. Schmidt, MD, Michael N. Wood, MD, and Edwin E. Vyhmeister, MD

Current Review

Current Concepts Concerning the Nature and Treatment of Barrett's Esophagus and Its Complications 586

John M. Streitz, Jr, MD, Warren A. Williamson, MD, and F. Henry Ellis, Jr, MD, PhD

Key References

Dynamic Cardiomyoplasty 592

Ray C.-J. Chiu, MD, PhD

Update

Combined Superior and Right Lateral Left Atriotomy with Division of the Superior Vena Cava for Exposure of the Mitral Valve 594

Hendrick B. Barner, MD

Correspondence

Profound Hypothermia and Circulatory Arrest 596

Eugène M. Baudet, MD

Reply

W. Gerald Rainer, MD

Extended Approach to the Mitral Valve 596

Arkalgud Sampathkumar, MD

Reply

Gerard M. Guiraudon, MD

Surgical Management of Carcinoid Heart Disease 598

Victor Aldrete, MD

Reply

Bruce B. Davis, MBBS, FACAS

Visualization of Coronary Artery Anastomoses by Gas Jet 598

Thomas J. Poulton, MD

Reply

Tomas A. Salerno, MD, and Kevin H. T. Teoh, MD

Balloon Angioplasty in the Treatment of Aortic Coarctation 599

Patrick L. Ergina, MD, and Christo I. Tchervenkov, MD

Reply

P. Syamasundar Rao, MD, and Paramjeet S. Chopra, MD

Homograft Root Replacement for Juvenile Rheumatoid Aortic Valve Incompetence 602

Paul Schoof, MD, Robert Jan van Suylen, MD, and Egbert Bos, MD, PhD

Reply

Samuel B. Keeley, MD

Internal Mammary Artery to Lung Parenchyma Fistula 603

Michael K. Wood, MD

Reply

Carlos Blanche, MD

Announcements

Information for Authors A-25, 26

Guidelines for the Submission of Electronic Manuscripts A-27

Forthcoming Articles A-28

Events of Interest A-31, 32

Notice From the American Board of Thoracic Surgery 583, 591

Thoracic Surgery Foundation for Research and Education 595

Correction 603

The Southern Thoracic Surgical Association: Thirty-ninth Annual Meeting 604

Program for the Thirty-ninth Annual Meeting of the Southern Thoracic Surgical Association 605

Classified Advertisements A-35, 36, 37

Index to Advertisers A-38

Number 4 October 1992

Original Articles

Cerebral Blood Flow and Metabolism in Hypothermic Circulatory Arrest 609

Craig K. Mezrow, MS, Ali M. Sadeghi, MD, Alejandro Gandsas, MD, Howard H. Shiang, DVM, Dale Levy, MD, Robert Green, MD, Ian R. Holzman, MD, and Randall B. Griepp, MD

Does a Posterior Aneurysm Increase the Risk of Endocardial Resection? 617

Irving L. Kron, MD, John A. Kern, MD, Pierre Theodore, BA, Terry L. Flanagan, MPH, David E. Haines, MD, Michael J. Barber, MD, and John P. DiMarco, MD, PhD

Anomalous Left Coronary Artery From the Pulmonary Artery: Results of Isolated Aortic Reimplantation 621

Pascal R. Vouhé, MD, Daniel Tamisier, MD, Daniel Sidi, MD, Françoise Vernant, MD, Philippe Mauriat, MD, Philippe Pouard, MD, and Francine Leca, MD

Anterior Mediastinal Tracheostomy With and Without Cervical Exenteration 628

Mark B. Orringer, MD

Postpneumonectomy Syndrome: Diagnosis, Management, and Results 638

Hermes C. Grillo, MD, Jo-Anne O. Shepard, MD, Douglas J. Mathisen, MD, and David J. Kanarek, MD

Revival of the Radial Artery for Coronary Artery Bypass Grafting 652

Christophe Acar, MD, Victor A. Jebara, MD, Michele Portoghese, MD, Bernard Beyssen, MD, Jean Yves Pagny, MD, Philippe Grare, MD, Juan C. Chachques, MD, Jean-Noël Fabiani, MD, Alain Deloche, MD, Jean Leon Guermonprez, MD, and Alain F. Carpentier, MD, PhD

Clinical and Hemodynamic Assessment of the Hancock II Bioprosthesis 661

Tirone E. David, MD, Susan Armstrong, MSc, and Zhao Sun, MA

Use of Epicardial Electrocardiograms for Detecting Cardiac Allograft Rejection 669

Eric D. Irwin, MD, Richard W. Bianco, BS, Rose Clack, BS, John Grehan, BA, David P. Slovut, MD, Raouf Nakhleh, MD, R. Morton Bolman III, MD, and Sara J. Shumway, MD

Predictive Criteria for the Need of Extracorporeal Circulation in Single-Lung Transplantation 676

Stephan W. Hirt, MD, Axel Haverich, MD, Thorsten Wahlers, MD, Hans-Joachim Schäfers, MD, Aiman Alken, MD, and Hans-Georg Borst, MD

Stentless Porcine and Pericardial Valve in Aortic Position 681

Riccardo Casabona, MD, Ruggero De Paulis, MD, Giuseppe F. Zattera, MD, Michele di Summa, MD, Walter Bottone, MD, Carla Stacchino, MD, Mario O. P. Vrandecic, MD, and Mario Morea, MD

Transhiatal Esophagectomy: A Safe Alternative for Selected Patients 686

Thomas M. Daniel, MD, Kirk J. Fleischer, MD, Terry L. Flanagan, MPH, Curtis G. Tribble, MD, and Irving L. Kron, MD

The Learning Curve for Intraoperative Echocardiography During Congenital Heart Surgery 691

Ross M. Ungerleider, MD, William J. Greeley, MD, Ronald J. Kanter, MD, and Joseph A. Kisslo, MD

Emergent Applications of Cardiopulmonary Support: A Multiinstitutional Experience 699

Jonathan G. Hill, MD, Pamela S. Bruhn, RN, BSN, Sheldon E. Cohen, MD, Michael W. Gallagher, MD, Frank Manart, MD, Charles A. Moore, MD, Paul E. Seifert, MD, Paul Askari, CCP, and Candace Banchieri, CCP

Effect of Light Dose on the Photodynamic Destruction of Endobronchial Tumors 705

James S. McCaughan, Jr, MD, Philip C. Hawley, MD, David G. Brown, MD, Gerard S. Kakos, MD, and Thomas E. Williams, Jr, MD

Nicardipine: Myocardial Protection in Isolated Working Hearts 712

Marc E. Mitchell, MD, David A. DeBoer, MD, Michael D. Crittenden, MD, and Richard E. Clark, MD

Electrophysiologic Study of Dysrhythmias After Atrial Operations in Dogs 717

Tatsuo Tamiya, MD, Toshiyuki Yamashiro, MD, Atsushi Hata, MD, Kenshi Kuge, MD, Sohichi Asano, MD, and Takayuki Sato, MD

Time for New Concepts About Measurement of Complement Activation by Cardiopulmonary Bypass? 725

Vibeke Videm, MD, PhD, Erik Fosse, MD, PhD, Tom Eirik Mollnes, MD, PhD, Peter Garred, MD, PhD, and Jan L. Svennevig, MD, PhD

Congenital Malformations of the Coronary Arteries: The Texas Heart Institute Experience 732

Eugene D. Fernandes, MD, Hooshang Kadivar, MD, Grady L. Hallman, MD, George J. Reul, MD, David A. Ott, MD, and Denton A. Cooley, MD

Exocrine Pancreatic Function in Mediastinal Teratomata: An Aid to Preoperative Diagnosis? 741

Panny Kallis, FRCS, Tom Treasure, FRCS, S. J. Keith Holmes, FRCS, and Meryl Griffiths, MRCPath

Endotoxin Release and Tumor Necrosis Factor Formation During Cardiopulmonary Bypass 744

Nicolaas J. G. Jansen, MD, PhD, Willem van Oeveren, PhD, Y. J. Gu, MD, Marilijn H. van Vliet, MD, Leon Eijsman, MD, PhD, and Charles R. H. Wildevuur, MD, PhD

Temperature Monitoring During CPB in Infants: Does It Predict Efficient Brain Cooling? 749

Frank H. Kern, MD, Richard A. Jonas, MD, John E. Mayer, Jr, MD, Frank L. Hanley, MD, Aldo R. Castaneda, MD, and Paul R. Hickey, MD

Surgical Management of Infective Endocarditis in Children 755

Michael Citak, MD, Allan Rees, MD, and Constantine Mavroudis, MD

Case Reports

Left Ventricular Diverticulum With Hypertrophy of the Left Ventricular Apex 761

Chojiro Yamashita, MD, Hiroomi Nakamura, MD, Satoshi Tobe, MD, Toshihiro Koterazawa, MD, and Sinnichirou Yamamoto, MD

Chronic Fibrosing Mediastinitis and Superior Vena Caval Obstruction From Blastomycosis 764

Carl F. Lagerstrom, MD, Holly G. Mitchell, MD, Barney S. Graham, MD, PhD, and John W. Hammon, Jr, MD

Saphenous Vein Graft Pseudoaneurysm Formation After Postoperative Mediastinitis 766

Julian A. Smith, FRACS, and Jacob Goldstein, FRACS

Unusual Complication of Temporary Pacing Wires in Children 769

Joe W. R. Bolton, MD, and John E. Mayer, Jr, MD

Aneurysm of Coronary Arteriovenous Fistula Presenting as a Calcified Mediastinal Mass 771

Yutaka Okita, MD, Shigehito Miki, MD, Kenji Kusuhara, MD, Yuichi Ueda, MD, Takafumi Tahata, MD, Tetsuro Sakai, MD, Akitoshi Tatsumi, MD, and Morihisa Kitano, MD

Bilateral Elastofibroma Dorsi 774

Hans-Günther Machens, MD, Ruth Mechtersheimer, MD, Ulrich Göhring, MD, and Peter N. Schlag, MD, PhD

Double-Lung Transplantation Using Donor Lungs With a Right Tracheal Bronchus 777

Pierre Y. Brichon, MD, Dominique Blin, MD, Ignacio Perez, MD, Christophe Pison, MD, François Blanc-Jouvan, MD, Isabelle Pin, MD, Didier Barnoud, MD, Elisabeth Brambilla, MD, and René Latreille, MD

Surgical Management of Left Coronary Artery Ostial Atresia and Supravalvar Aortic Stenosis 779

Eliot R. Rosenkranz, MD, Daniel J. Murphy, Jr, MD, and Delos M. Cosgrove III, MD

Hyperbaric Oxygen: Value in Management of Nonhealing Saphenectomy Wounds 782

Michael D. Horowitz, MD, Carmen G. Portogues, PA, Luis A. Matos, MD, and Robert W. McGowan III, PA

Pericardial Repair of a Tracheal Laceration During Transhiatal Esophagectomy 784

Lyall A. Gorenstein, MD, James G. Abel, MD, and G. Alexander Patterson, MD

How to Do It

Limited Vertical Skin Incision for Median Sternotomy 787

Shoh Tatebe, MD, Shoji Eguchi, MD, Haruo Miyamura, MD, Satoshi Nakazawa, MD, Hiroshi Watanabe, MD, Masa-aki Sugawara, MD, Jun-ichi Hayashi, MD, Kazutoshi Date, MD, and Satoru Nakagawa, MD

Directed Atraumatic Coronary Sinus Cannulation for Retrograde Cardioplegia Administration 789

Gabriel S. Aldea, MD, Gilbert Connelly, MD, James D. Fonger, MD, Dusan Dobnik, MD, and Richard J. Shemin, MD

Bilateral Anterior Thoracotomy for Automatic Implantable Cardioverter Defibrillator Placement in Patients With Previous Sternotomy 791

Shreekanth V. Karwande, MD, and John R. Rowles, MD

New Side-Holed Sheath for Intraaortic Balloon Pumping to Maintain Limb Perfusion 794

Hisashi Satoh, MD, Tohru Kobayashi, MD, Taizou Hiraishi, MD, Makoto Sakurai, MD, Yoshiyuki Fudemoto, MD, Mitsunori Kaneko, MD, Susumu Nakano, MD, and Hikaru Matsuda, MD

New Surgical Technique for Type B Aortic Interruption 797

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Fadel Al-Fadley, FRCP(C), Zohair Al-Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

Current Review

Video-Assisted Thoracic Surgery: Basic Technical Concepts and Intercostal Approach Strategies 800

Rodney J. Landreneau, MD, Michael J. Mack, MD, Stephen R. Hazelrigg, MD, Robert D. Dowling, MD, Tea E. Acuff, MD, Mitchell J. Magee, MD, and Peter F. Ferson, MD

Update

Chemoradiation Therapy and Resection for Carcinoma of the Esophagus: Short-term Results 808

Edward F. Parker, MD

Correspondence

Esophageal Perforation 809

Safuh Attar, MD

Reply

William G. Jones II, MD, and Robert J. Ginsberg, MD

Ross' First Homograft Replacement of the Aortic Valve 809

Alfred J. Gunning, FRCS

Reply

Richard A. Hopkins, MD

Reply

Donald Ross, FRCS

Continuous Normothermic Blood Cardioplegia: Simplified Delivery Circuit 810

Ponangi V. Satyanarayana, MS, MCh, Podila Sita Rama Rao, MS, MCh, Kesavaram Madhusudhana Rao, BSc, CCP, Alluru Sarath Chandra, MS, Kanchumarthi Sudhakar Rao, MS, and Karri Venkat Reddy, MS

Thromboelastogram and Postoperative Hemorrhage 810

Bruce D. Spiess, MD

Kenneth J. Tuman, MD, Robert J. McCarthy, PharmD, and Anthony D. Ivankovich, MD

Paul G. Martin, BSc, Ferenc Horkay, MD, Nirmal K. Gupta, MCh, and Duncan R. Walker, FRCS

Reply

Chung-Yuan Lin, MD, and Jian-Sheng Wang, MD

Palliative Intubation for Dysphagia 813

Lewis Wetstein, MD

Reply

Theodore K. Liakakos, MD, Sunil K. Ohri, FRCS, Edward R. Townsend, FRCS, and
S. William Fountain, FRCS

The Blue Man Phenomenon 814

Ian M. Mitchell, FRCS, Nigel R. Saunders, FRCS, Robert D. Paton, PhD, and
Robert W. Logan, FRCP(Glasg)

Minimal Hemodilution and Optimal Potassium Use During Normothermic Aerobic Arrest 815

Daniel Le Houerou, MD, Ajoy I. Singh, MD, Mauro Romano, MD, Victor Martin, MD,
and Arrigo Lessana, MD

Rapid Transfusion After Aortic Decannulation 816

Jose M. Bernal, MD, Jose M. Rabasa, MD, and Jose M. Revuelta, MD

Review of Recent Books

Mediastinal Surgery, edited by Thomas W. Shields, MD 781

James L. Nielsen, MD

Announcements

Forthcoming Articles A-26

Information for Authors A-27, 28

Guidelines for the Submission of Electronic Manuscripts A-29

Events of Interest A-30, 31

Notice From The Society of Thoracic Surgeons 675

Notice From the Southern Thoracic Surgical Association 740

Notice From the American Board of Thoracic Surgery 783, 793

Classified Advertisements A-33, 34, 35

Index to Advertisers A-42

Number 5 November 1992

Editorial

Allogenic Vein as a Conduit for Coronary Artery Bypass 817

Hendrick B. Barner, MD

Thoracic Surgery Directors Association Award

Intrathecal Perfusion of an Oxygenated Perfluorocarbon Prevents Paraplegia After Aortic Occlusion 818

Robert E. Maughan, MD, Chittur Mohan, MD, Ira M. Nathan, PhD, Enrico Ascer, MD, Peter Damiani, BS, Israel J. Jacobowitz, MD, Joseph N. Cunningham, Jr, MD, and Corrado P. Marini, MD

Original Articles

Cryopreserved Allograft Veins as Alternative Coronary Artery Bypass Conduits: Early Phase Results 826

Glenn W. Laub, MD, S. Muralidharan, MD, Robert Clancy, RN, W. Jay Eldredge, MD, Chao Chen, PhD, Mark S. Adkins, MD, Javier Fernandez, MD, William A. Anderson, MD, and Lynn B. McGrath, MD

Late Results of Operation for Ventricular Tachycardia 832

Lynda L. Mickleborough, MD, Shun-ichi Mizuno, MD, Eugene Downar, MD, and Gordon C. Gray, BSc

Cardiac Retransplantation: A Viable Option? 840

Shreekanth V. Karwande, MD, R. Douglas Ensley, MD, Dale G. Renlund, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, Donald B. Doty, MD, M. Elizabeth Hammond, MD, John D. Marks, PE, and The Registry of the International Society for Heart and Lung Transplantation

Acute Rejection of Lung Allografts With Various Immunosuppressive Protocols 846

Bartley P. Griffith, MD, Robert L. Hardesty, MD, John M. Armitage, MD, Robert L. Kormos, MD, Gary C. Marrone, MD, Steve Duncan, MD, Irvin Paradis, MD, James H. Dauber, MD, Samuel A. Yousem, MD, and Penny Williams, MD

Improved Myocardial Ischemic Tolerance by Contractile Inhibition With 2,3-Butanedione Monoxime 852

James C. Stringham, MD, Karen L. Paulsen, BS, James H. Southard, PhD, Barry L. Fields, MD, and Folkert O. Belzer, MD

Extracorporeal Membrane Oxygenation for Cardiac Failure After Congenital Heart Operation 861

Stanley Ziomek, MD, James E. Harrell, Jr, MD, James W. Fasules, MD, Sherry C. Faulkner, CCP, Carl W. Chipman, RN, Michele Moss, MD, Elizabeth Frazier, MD, and Stephen H. Van Devanter, MD

Coarctation of the Aorta in Infants: Does the Aortic Arch Grow After Repair? 869

John L. Myers, MD, Brian A. McConnell, BS, and John A. Waldhausen, MD

Postinfarct Ventricular Septal Defect Repair: Effect of Coronary Artery Bypass Grafting 876

Derek D. Muehrcke, MD, Willard M. Daggett, Jr, MD, Mortimer J. Buckley, MD, Cary W. Akins, MD, Alan D. Hilgenberg, MD, and W. Gerald Austen, MD

Risk Analysis of Operative Intervention for Failed Coronary Angioplasty 884

A. Michael Borkon, MD, Trent L. Failing, MD, Jeffrey M. Piehler, MD,
Duncan A. Killen, MD, Marcia L. Hoskins, BS, and William A. Reed, MD

Partial Median Sternotomy for Repair of Heart Defects: A Cosmetic Approach 892

William R. Wilson, Jr, MD, Michel N. Ilbawi, MD, Serafin Y. DeLeon, MD,
William Piccione, Jr, MD, Kate Tubeszewski, RN, MSN, and Anthony F. Cutilletta, MD

Surgical Considerations in Bypassing Coronary Arteries With 100% Proximal Occlusion 894

Thomas R. McLean, MD, Lars G. Svensson, MD, PhD, Bernardo Stein, MD,
Arthur C. Beall, Jr, MD, and John I. Thornby, PhD

Role of Open Lung Biopsy in Diagnosing Pulmonary Complications of AIDS 898

Gregory D. Trachiotis, MD, Gordon H. Hafner, MD, William R. Hix. MD, and
Benjamin L. Aaron, MD

Tetralogy of Fallot: Favorable Outcome of Nonneonatal Transatrial, Transpulmonary Repair 903

Tom R. Karl, MD, Shunji Sano, MD, PhD, Samphant Pornviliwan, MD, and
Roger B. B. Mee, FRACS

Benefits of Combined Balloon Pumping and Percutaneous Cardiopulmonary Bypass 908

Steven J. Phillips, MD, Robert H. Zeff, MD, Chamnahn Kongtahworn, MD,
André Grignon, MD, Lawrence Barker, RN, L. A. Iannone, MD,
Mark Tannenbaum, MD, Margaret H. Verhey, MD, William J. Wickemeyer, MD,
Magdi G. Ghali, MD, and David F. Gordon, MD

Coronary Artery Bypass Using Internal Mammary Artery Branches 911

Jean E. Morin, MD, Giles Hedderich, MD, Normand L. Poirier, MD, John Sampalis, PhD,
and James F. Symes, MD

Isolated Biventricular Working Rat Heart Preparation 915

Todd L. Demmy, MD, George J. Magovern, MD, and Race L. Kao, PhD

Effect of Prostaglandin I_2 and Superoxide Dismutase on Reperfusion Injury of Warm Ischemic Lung 921

Chojiro Yamashita, MD, Hidefumi Oobo, MD, Fukumasa Tsuji, MD, Satosi Tobe, MD,
Hidehiro Yamamoto, MD, Hiroomi Nakamura, MD, Masayosi Okada, MD, and
Kazuo Nakamura, MD

Comparison of 180-Degree and 360-Degree Skeletal Muscle Nerve Cuff Electrodes 925

George V. Letsou, MD, James F. Hogan, BSEE, Philip Lee, MS, Jung H. Kim, MD,
Stephan Ariyan, MD, Michael L. Dewar, MD, John C. Baldwin, MD, and
John A. Elefteriades, MD

Technique of Open Distal Anastomosis for Repair of Descending Thoracic Aortic Aneurysms 932

Denton A. Cooley, MD, and Robert T. Baldwin, MD

Expanding Wire Stents in Benign Tracheobronchial Disease: Indications and Complications 937

Samer A. M. Nashef, FRCS, Claire Dromer, MD, Jean-François Velly, MD, Louis Labrousse, MD, and Louis Couraud, MD

Extrapleural Pneumonectomy in the Treatment of Malignant Pleural Mesothelioma 941

David J. Sugarbaker, MD, Steven J. Mentzer, MD, and Gary Strauss, MD

Considerations in the Skeletonization Technique of Internal Thoracic Artery Dissection 947

James M. Cunningham, MD, Mohammad A. Gharavi, MD, Rostam Fardin, MD, and Raymond A. Meek, MD

The Meadox-Gabbay Pericardial Xenograft: Failure of the Unicusp Principle 952

Uberto Bortolotti, MD, Paolo Ius, MD, Gaetano Thiene, MD, Marco Minarini, BS, Aldo Milano, MD, Carlo Valfrè, MD, Enrico Talenti, MD, Marialuisa Valente, MD, and Alessandro Mazzucco, MD

Comparison of Cardiac Output Measured by Intrapulmonary Artery Doppler, Thermodilution, and Electromagnetometry 959

Paul M. Heerdt, MD, PhD, Charles G. Pond, MD, George A. Blessios, MD, and Michael Rosenbloom, MD

Pulmonary Artery Sling 967

Ashwinikumar Pawade, FRCS, Marc R. de Leval, FRCS, Martin J. Elliott, FRCS, and Jaroslav Stark, FRCS

Case Reports

Pulmonary Artery Sling With Tracheal Stenosis: Primary One-Stage Repair in Infancy 971

Gerhard Ziemer, MD, Markus Heinemann, MD, Renate Kaulitz, MD, Joachim Freihorst, MD, Jürgen Seidenberg, MD, and Martin Wilken, MD

Surgically Created Wolff-Parkinson-White Syndrome After Fontan Operation 974

Anees J. Razzouk, MD, Robert Gow, MB, BS, John Finley, MD, David Murphy, MD, and William G. Williams, MD

True Aneurysm of the Saphenous Vein Graft Stump Associated With CABG in a Cardiac Transplant Patient 978

Robert T. Baldwin, MD, Tomas Klima, MD, O. H. Frazier, MD, James Lonquist, MD, and Branislav Radovancevic, MD

Chronic, Traumatic Pseudoaneurysm of the Ascending Aorta 980

Felipe C. Albuquerque, BA, Mark J. Krasna, MD, and Joseph S. McLaughlin, MD

Aneurysm of the Ascending Aorta After Cardiac Transplantation 983

Jean-Olivier Defraigne, MD, Olivier Vahdat, MD, Jean-Paul Lavigne, MD, Jean-Claude Demoulin, MD, PhD, and Raymond Limet, MD, PhD

Simplified Correction of Outflow Obstruction After Mitral Valve Replacement 985

Mark K. Reed, MD, and Leigh I. G. Iverson, MD

Bronchoenteric Fistula From an Infected Internal Cardioverter Defibrillator 987

Peter L. Birnbaum, MD, Samuel V. Lichtenstein, MD, PhD, William H. Noble, MD, Benjamin G. Guslits, MD, Brian D. Kenney, MD, D. Ian Soutter, MD, Anthony L. Panos, MD, Paul Dorian, MD, and David Newman, MD

Total Correction of Transposition of Great Arteries With Atrioventricular Septal Defect 989

Naresh Kumar, FRCS, Ganga Prabhakar, FRCS, Neil Wilson, MRCP, DCH, Zohair Al Halees, FRCS(C), and Carlos M. G. Duran, MD, PhD

How to Do It

New Surgical Technique for Total-Defect Aortopulmonary Window 991

Osamu Matsuki, MD, Toshikatsu Yagihara, MD, Fumio Yamamoto, MD, Kyoichi Nishigaki, MD, Hideki Uemura, MD, and Yasunaru Kawashima, MD

Newly Developed Holder for a Right-Angled Metal Venous Cannula 993

Takashi Watanabe, MD, Toshio Abe, MD, Minoru Tanaka, MD, Kenzo Yasuura, MD, Hiroshi Hikosaka, MD, Yoshito Suenaga, MD, and Hidekazu Hosokawa, MD

Modified Urinary Collecting Bags for Prolonged Underwater Chest Drainage 995

Yaron Bar-El, MD, Yair Lieberman, MD, and Alon Yellin, MD

Classics in Thoracic Surgery

Clarence Crafoord and the First Successful Resection of a Cardiac Myxoma 997

W. Randolph Chitwood, Jr, MD

Current Review

Surgical Treatment for Higher Stage Non–Small Cell Lung Cancer 999

Dirk E. Van Raemdonck, MD, Airton Schneider, MD, and Robert J. Ginsberg, MD

Key References

Aortic Valve Repair 1014

Delos M. Cosgrove III, MD

Update

A Method for Predicting Postoperative Lung Function and Its Relation to Postoperative Complications in Patients with Lung Cancer 1016

Kazuya Nakahara, MD, Shinichiro Miyoshi, MD, and Katuhiro Nakagawa, MD

Correspondence

Aprotinin Treatment During Open Heart Operation in a Patient With Severe Thrombocytopenia 1018

Ehud Deviri, MD, Uzi Izhar, MD, Benjamin Drenger, MD, Yitzhak Glick, MD, and Joseph B. Borman, FRCS(Eng)

Thermo Cardiosystems Left Ventricular Assist Device 1019

O. H. Frazier, MD

Reply

Nelson A. Burton, MD, W. Stephen Phillips, MD, Quentin Macmanus, MD, and Edward A. Lefrak, MD

Plateletpheresis and Transfusion Practice in Heart Operations 1020

Gerald G. Davies, FFARCSI, Douglas G. Wells, FFARACS, Richard Sadler, MD, Thomas M. Mabee, MD, Mitchell Ruffcorn, MD, and John B. Dooley, MD

Preoperative Morphologic and Physiologic Assessment of Internal Thoracic Arteries 1020

Charles C. Canver, MD

Reply

Frederick L. Grover, MD

Manual Versus Stapled Bronchial Closure: Still Controversial 1021

Rafael Aguilo, MD, and Miguel Llobera, MD, PhD

Reply

L. Penfield Faber, MD, S. Russell Vester, MD, C. Frederick Kittle, MD, William H. Warren, MD, and Robert J. Jensik, MD

High-Dose Aprotinin in Emergency Coronary Artery Bypass After Thrombolysis 1022

Franco Alajmo, MD, and Giancarlo Calamai, MD

Reply

Theodore Efstratiadis, MD, PhD, Christopher Munsch, ChM, David Crossman, MB, and Kenneth M. Taylor, MD

Hemodynamic Effects of Pericardial Closure 1023

Arkalgud Sampathkumar, MD

Reply

Steven Hunter, FRCS, and Gianni D. Angelini, MD

Abrupt Cardiac Failure Using a Right VAD in the Presence of a Tricuspid Valve Prosthesis 1023

Steven C. Griffin, FRCS, and John H. Dark, FRCS

Review of Recent Books

A Textbook of Cardioplegia for Difficult Clinical Problems, edited by Richard M. Engelman, MD, and Sidney Levitsky, MD 994

Edward Y. Sako, MD, PhD

Cardiac and Noncardiac Complications of Open Heart Surgery: Prevention, Diagnosis and Treatment, edited by Morris N. Kotler, MD, and Anthony Alfieri, DO 1015

James L. Nielsen, MD

Announcements

Information for Authors A-25, 26

Guidelines for the Submission of Electronic Manuscripts A-27

Events of Interest A-28, 29

Forthcoming Articles A-30

Notice From The Society of Thoracic Surgeons 860

Notice From the American Board of Thoracic Surgery 946, 982

Classified Advertisements A-31, 32, 33

Index to Advertisers A-40

Number 6 December 1992

J. Maxwell Chamberlain Memorial Paper

Fontan Procedure for Hypoplastic Left Heart Syndrome 1025

William I. Norwood, Jr, MD, PhD, Marshall L. Jacobs, MD, and John D. Murphy, MD

Original Articles

Aprotinin Therapy for Reoperative Myocardial Revascularization: A Placebo-Controlled Study 1031

Delos M. Cosgrove III, MD, Blaine Heric, MD, Bruce W. Lytle, MD, Paul C. Taylor, MD, Roberto Novoa, MD, Leonard A. R. Golding, MD, Robert W. Stewart, MD, Patrick M. McCarthy, MD, and Floyd D. Loop, MD

Mediastinitis in Heart Transplantation 1039

Shreekanth V. Karwande, MD, Dale G. Renlund, MD, Stephanie L. Olsen, MD, William A. Gay, Jr, MD, Wayne E. Richenbacher, MD, John A. Hawkins, MD, Roger C. Millar, MD, and John D. Marks, PE

Long-Term Effect of Total Fundoplication on the Myotomized Esophagus 1046

Philippe Topart, MD, Claude Deschamps, MD, Raymond Taillefer, MD, and André Duranceau, MD

Clinical Manifestation of Mediastinal Fibrosis and Histoplasmosis 1053

Douglas J. Mathisen, MD, and Hermes C. Grillo, MD

Postcardiotomy Centrifugal Mechanical Ventricular Support 1059

Leonard A. R. Golding, MD, Ray D. Crouch, MD, Robert W. Stewart, MD, Roberto Novoa, MD, Bruce W. Lytle, MD, Patrick M. McCarthy, MD, Paul C. Taylor, MD, Floyd D. Loop, MD, and Delos M. Cosgrove III, MD

Device-Supported Myocardial Revascularization: Safe Help for Sick Hearts 1065

Michael S. Sweeney, MD, and O. H. Frazier, MD

Early Cellular Events in the Lung Allograft 1071

Riad Adoumie, MD, Cyril Serrick, BS, Adel Giaid, PhD, and Hani Shennib, MD

Bioassay of EDRF From Internal Mammary Arteries: Implications for Early and Late Bypass Graft Patency 1078

Paul J. Pearson, MD, PhD, Paulo R. B. Evora, MD, PhD, and Hartzell V. Schaff, MD

Coronary Artery Bypass Without Cardiopulmonary Bypass 1085

Albert J. Pfister, MD, M. Salah Zaki, MD, Jorge M. Garcia, MD, Luis A. Mispireta, MD, Paul J. Corso, MD, Anjum G. Qazi, MD, Steven W. Boyce, MD, Thomas R. Coughlin, Jr, MD, and Patricia Gurny, MD

Left Atrial Isolation Associated With Mitral Valve Operations 1093

Angelo Graffigna, MD, Francesco Pagani, MD, Gaetano Minzioni, MD, Jorge Salerno, MD, and Mario Viganò, MD

Combined Carotid and Coronary Revascularization: The Preferred Approach to the Severe Vasculopath 1099

Robert J. Rizzo, MD, Anthony D. Whittemore, MD, Gregory S. Couper, MD, Magruder C. Donaldson, MD, Sary F. Aranki, MD, John J. Collins, Jr, MD, John A. Mannick, MD, and Lawrence H. Cohn, MD

Vascular Anatomy of the Gastric Tube Used for Esophageal Reconstruction 1110

Dorothea M. I. Liebermann-Meffert, MD, Renate Meier, MD, and J. Rüdiger Siewert, MD

Absent Pulmonary Valve Syndrome: Operation in Infants With Airway Obstruction 1116

Kevin G. Watterson, FRACS, Torsten K. Malm, MD, PhD, Tom R. Karl, MD, and Roger B. B. Mee, FRACS

Effect of Delay in Retroperfusion Therapy on Infarct Size Reduction 1120

Christopher M. Feindel, MD, Reena Sandhu, MSc, Jorge Cruz, MD, and Gregory J. Wilson, MSc, MD

Hyperglycemia Increases Cerebral Intracellular Acidosis During Circulatory Arrest 1126

Richard V. Anderson, MD, Michael G. Siegman, MD, Robert S. Balaban, PhD, Toni L. Ceckler, PhD, and Julie A. Swain, MD

Barbiturates Impair Cerebral Metabolism During Hypothermic Circulatory Arrest 1131

Michael G. Siegman, MD, Richard V. Anderson, MD, Robert S. Balaban, PhD, Toni L. Ceckler, PhD, Richard E. Clark, MD, and Julie A. Swain, MD

Coronary Sinus Injuries During Retrograde Continuous Normothermic Blood Cardioplegia 1137

Anthony L. Panos, MD, Imtiaz S. Ali, MD, Peter L. Birnbaum, MD,
Carlos A. M. Barrozo, MD, Owayed Al-Nowaiser, MD, and Tomas A. Salerno, MD

Clinical Cardiomyoplasty: Preoperative Factors Associated With Outcome 1139

Anthony P. Furnary, MD, James A. Magovern, MD, Ignacio Y. Christlieb, MD,
Judith E. Orie, MD, Kathleen A. Simpson, BS, and George J. Magovern, MD

Fluosol Cardioplegia Results in Complete Functional Recovery: A Comparison With Blood Cardioplegia 1144

Jeffrey M. Pearl, MD, Hillel Laks, MD, Davis C. Drinkwater, MD, Avedis Meneshian, BS,
Steven M. Martin, MD, Mark Curzan, MS, and Paul A. Chang, BS

Influence of β_1-Blockade on Myocardial Substrates Early After a Coronary Operation 1151

Örjan Wesslén, MD, Jan van der Linden, MD, Rolf Ekroth, MD,
Per-Olof Joachimsson, MD, Lars Nordgren, MD, Sven-Olov Nyström, MD,
Gunnar Ronquist, MD, and Hans Tydén, MD

Pleuropulmonary Aspergilloma: Clinical Spectrum and Results of Surgical Treatment 1159

Gilbert Massard, MD, Norbert Roeslin, MD, Jean-Marie Wihlm, MD, Pascal Dumont, MD,
Jean-Paul Witz, MD, and Georges Morand, MD

Temporary Double Exclusion of the Perforated Esophagus Using Absorbable Staples 1165

Romeo Bardini, MD, Luigi Bonavina, MD, Maurizio Pavanello, MD, Massimo Asolati, MD,
and Alberto Peracchia, MD

Vascular and Interstitial Effect of University of Wisconsin Solution on Canine Lung 1168

Helmut W. Unruh, MD

Low-Dose Aprotinin in Internal Mammary Artery Bypass Operations Contributes to Important Blood Saving 1172

Jacques P. A. M. Schönberger, MD, Peter A. M. Everts, EKP, Husam Ercan, MD,
Johan J. Bredée, MD, PhD, Johan H. Bavinck, MD, Eric Berreklouw, MD, and
Charles R. M. Wildevuur, MD, PhD

Safety and Efficacy of Autologous Blood Donation Before Elective Aortic Valve Operation 1177

Walter H. Dzik, MD, Arlen G. Fleisher, MD, David Ciavarella, MD, Karl J. Karlson, MD,
George E. Reed, MD, and Robert L. Berger, MD

Clinical and Hemodynamic Evaluation of the 19-mm Carpentier-Edwards Supraannular Aortic Valve 1182

Panny Kallis, FRCS, James F. Sneddon, MRCP, Iain A. Simpson, MRCP,
Anthony Fung, FRCS, John R. Pepper, FRCS, and E. E. John Smith, FRCS

Optimal Approach to the Mitral Valve: Dissection of the Interatrial Groove 1186

Robert I. Larbalestier, MD, Richard B. Chard, FRCS, and Lawrence H. Cohn, MD

Pulmonary "Twinning" Procedure: Use of Lungs From One Donor for Single-Lung Transplantation in Two Recipients 1189

David A. Haydock, MD, Donald E. Low, MD, Elbert P. Trulock, MD,
Larry R. Kaiser, MD, Michael K. Pasque, MD, Ernesto Molmenti, MD, and
Joel D. Cooper, MD

Radical Laser Segmentectomy for T1 N0 Lung Cancer 1193

Ken Kodama, MD, Osamu Doi, MD, Takushi Yasuda, MD, Masahiko Higashiyama, MD,
and Hideoki Yokouchi, MD

Quantitation of Particulate Microemboli During Cardiopulmonary Bypass: Experimental and Clinical Studies 1196

Jin-Feng Liu, MD, Zhao-Kang Su, MD, and Wen-Xiang Ding, MD

Case Reports

Complete Cure After a Seemingly Unsuccessful Operation for Wolff-Parkinson-White Syndrome 1203

Peter Rakovec, MD, DSc, Aleš Brecelj, MD, and Igor Zupan, MD

Pneumatocele Complicating Hyperimmunoglobulin E Syndrome (Job's Syndrome) 1206

Robert C. Shamberger, MD, Mary Ellen Wohl, MD, Antonio Perez-Atayde, MD, and
W. Hardy Hendren, MD

Surgical Treatment of Postinfarction Ventricular Septal Defect With Aortic Stenosis 1209

Lauren R. Boglioli, BS, Thomas A. Traill, MRCP, Alfred S. Casale, MD,
Bruce A. Reitz, MD, and Duke E. Cameron, MD

Pleural Liposarcoma Presenting With Respiratory Distress and Suspected Diaphragmatic Hernia 1212

Francis Carroll, MD, Marshall D. Kramer, MD, Anthony J. Acinapura, MD,
Patricia A. Tietjen, MD, Ira Wagner, MD, Stanley Oiseth, MD, and Fred Smith, MD

Retrograde Coronary Sinus Cardioplegia in the Presence of Persistent Left Superior Vena Cava 1214

David M. Shahian, MD

Post-Atherectomy Coronary Artery Aneurysm 1216

Amram J. Cohen, MD, Alan Banks, MD, Patrick Cambier, MD, and Fred H. Edwards, MD

Giant Intrapericardial Solitary Fibrous Tumor 1219

Uberto Bortolotti, MD, Francesco Calabrò, MD, Monica Loy, MD, Giuseppe Fasoli, MD,
Giuseppe Altavilla, MD, and Domenico Marchese, MD

Management of Severe Bronchial Ischemia After Bilateral Sequential Lung Transplantation 1221

Derya Oturanlar, MD, Walter Klepetko, MD, Michael Grimm, MD, Adelheid End, MD,
Wilfried Wisser, MD, Thomas Wekerle, MD, and Ernst Wolner, MD

How to Do It

Permanent Pacemaker Implantation in Premature Infants Less Than 2,000 Grams of Body Weight 1223

Mikio Ohmi, MD, Motohisa Tofukuji, MD, Kaori Sato, MD, Takahiko Nakame, MD, Naoshi Sato, MD, Kiyoshi Haneda, MD, and Hitoshi Mohri, MD

Replacement of Paracorporeal Ventricular Assist Devices 1226

Douglas P. Lohmann, ME, Lawrence R. McBride, MD, D. Glenn Pennington, MD, and Marc T. Swartz, BA

Inverted Y Incision for Accurate Tailoring of Patches and Vessels 1228

Darryl M. Hoffman, FRCS, and Robert W. M. Frater, FRCS

Repairing the Degenerative Anterior Mitral Leaflet 1229

John M. Alvarez, FRACS, Narcissus Teoh, MB, BS, and Cedric W. Deal, FRACS

Classics in Thoracic Surgery

The Nissen Fundoplication 1231

F. Henry Ellis, Jr, MD, PhD

Current Review

Release of Vasoactive Substances During Cardiopulmonary Bypass 1236

Stephen W. Downing, MD, and L. Henry Edmunds, Jr, MD

Correspondence

Team Approach for Clinical Cardiac Surgery Research 1244

Charles C. Canver, MD, and Roger C. Fiedler, PhD

Length of the In Situ Right Gastroepiploic Artery for Coronary Artery Bypass 1244

Giuseppe Tavilla, MD

Reply

Hisayoshi Suma, MD

Electrical Instability During Reperfusion 1245

William L. Holman, MD

Pulmonary Pseudotumor 1246

Hussam A. Fadhli, MD

Hemolysis After Open Heart Operations 1246

Alessandro Golino, MD, Paolo Stassano, MD, and Nicola Spampinato, MD

Reply

Yutaka Okita, MD, and Shigehito Miki, MD

Penetrating Cardiac Trauma 1247

Rao R. Ivatury, MD, and Michael Rohman, MD

Reply

Christopher J. Knott-Craig, MD

Surgery of Aortic Dissections With GRF Glue 1248

Harald E. Zeplin, MD

Modified Retractor to Prevent Peripheral Nerve Injury 1249

Nelson Ancalmo, MD

Announcements

Information for Authors A-31, 32

Guidelines for the Submission of Electronic Manuscripts A-33

Events of Interest A-34, 35

Forthcoming Articles A-37

Notice From The Society of Thoracic Surgeons 1181

Notice From the American Board of Thoracic Surgery 1205, 1215

The Society of Thoracic Surgeons: Twenty-ninth Annual Meeting 1250

Twenty-sixth Postgraduate Program, The Society of Thoracic Surgeons 1251

Program for the Twenty-ninth Annual Meeting of The Society of Thoracic Surgeons 1252

Classified Advertisements A-39, 40, 41

Index to Advertisers A-42

Index to Volume 54

Author Index 1265

Subject Index 1285

CLASSIFIED ADVERTISEMENTS

Classified advertisements for positions wanted or available must relate only to the thoracic or cardiovascular surgical specialties. Display space (minimum, ¼ page) is also available through Art Carlucci, Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010 (telephone: (212) 633-3806; facsimile: (212) 633-3820). All advertisements are subject to the approval of the editor, and material deemed inappropriate for publication in *The Annals* will be rejected. If anonymity is desired, please indicate this at the time of submission and a code number will be assigned. All responses received will remain confidential in the publisher's office and will be conveyed to the advertiser shortly after receipt. The charge for all classified advertising is **$1.50 per word per insertion, minimum 20 words.** Abbreviations, dates, initials, post office box numbers, telephone numbers, years, and zip codes are considered one word each. **There is an additional fee of $18.00 per insertion for box number advertisements.** The copy deadline is 7 weeks prior to publication, eg, for the March issue, copy should be received by the 1st of January. Advertisement orders should be for a maximum of 6 months; advertisements may be renewed for up to 6 months at a time. Advertisement copy should be typed double-spaced and mailed in duplicate to: *The Annals of Thoracic Surgery,* Desk Editorial, Classified Advertisements, Elsevier Science Publishing Co, Inc, 655 Avenue of the Americas, New York, NY 10010 (facsimile: (212) 633-3853). Make *nonrefundable* check payable to Elsevier Science Publishing Co, Inc.

Please note that *The Annals* does not function as a placement service and cannot provide information on advertised positions. When answering advertisements, please write individually to each advertiser you wish to contact, using the address given in the advertisement. To respond to an anonymous advertisement, write to Box Number, *The Annals of Thoracic Surgery,* Elsevier Science Publishing, 655 Avenue of the Americas, New York, NY 10010.

SITUATIONS AVAILABLE

Thoracic and cardiovascular surgeon with emphasis on pediatric/neonate cardiac surgery and cardiac transplantation is needed by a full-service thoracic and cardiovascular surgery group on the west coast. Must have ABTS certification. Excellent salary and benefits package. Please respond with curriculum vitae and case list.

Please respond to Box 702. 702K/D

Cardiothoracic surgeon, board certified/eligible, wanted to join established practice in northwest Indiana (very near Chicago). Excellent salary. Please respond with curriculum vitae.

Please respond to Box 723. 723L/G

Cardiothoracic and vascular surgeon, BE/BC, to join a well-established, very busy private practice in New England. Medical school affiliation. Excellent salary and benefits with eventual partnership.

Please respond to Box 727. 727G/L

Cardiovascular surgeon, board certified/eligible, wanted to join two surgeons in an established cardiovascular program in the southeastern USA. Must have experience in adult cardiac, thoracic, and vascular surgical procedures. Salary/full partnership negotiable. Please send resume.

Please respond to Box 728. 728G/L

Cardiothoracic surgeon, BE/BC, wanted to join established practice in mid-Michigan group of two. Ninety percent of practice is adult surgery and ten percent is general thoracic surgery. Respond with CV and names of references.

Please respond to Box 735. 735G/L

Board eligible or certified cardiovascular and thoracic surgeon needed to join a busy practice in the Southeast. Excellent salary and fringe benefits leading to partnership.

Please respond to Box 737. 737H/A

Cardiothoracic vascular surgeon, board certified or board eligible, to join well-established, busy one-man private practice in Midwest. Salary leading to partnership. Please send CV and references.

Please respond to Box 743. 743H/A

BC/BE cardiovascular and thoracic surgeon wanted to join busy two-member group in Fort Lauderdale, Florida. Recent US medical graduate preferred.

Please send CV to I. Tabry, MD, 2773 NE 37th Drive, Fort Lauderdale, FL 33308 ((305) 561-9781 after 9:00 PM). 746H/A

Cardiothoracic and vascular surgeon, board eligible or certified, to join 2-man private practice in Ft. Lauderdale, Florida.

Please send CV to Salem M. Habal, MD, 4800 NE 20th Terrace #107, Ft. Lauderdale, FL 33308; (305) 771-3220. 748H/A

Cardiothoracic surgeon, BC/BE, wanted to join adult cardiac surgery program in the South. Solo practice is very busy serving as regional referral center. First-rate medical facilities, liberal compensation package, and warm hospitality await you! Please send CV.

Please respond to Box 752. 752I/L

Thoracic/cardiovascular surgeon: three-man group in suburban New York doing general thoracic and peripheral vascular surgery desires new graduate of approved thoracic program with training in vascular surgery. Please respond with CV.

Please respond to Box 758. 758I/B

Cardiovascular and thoracic surgeon: BE/BC wanted to join an established, busy private practice in the Midwest. Peripheral vascular expertise desirable. Recent graduate of a university program preferred. Salary leading to full partnership. Please respond with curriculum vitae and references.

Please respond to Box 763. 763I/B

Cardiothoracic surgeon—BE/BC—to join 2-man practice in South performing adult cardiac, thoracic, and vascular surgery. Surgeon finishing training or recent graduate preferred.

Please respond to Box 770. 770J/A

Cardiothoracic and vascular surgeon to join a busy and well-established 3-man practice in mid-Michigan. Applicant should be board certified or eligible in thoracic and cardiovascular surgery. We prefer a candidate who has recently completed his or her training. Competitive salary leading to early partnership, with excellent benefits and working conditions. Please respond with CV.

Please respond to Box 772. 772J/L

Cardiovascular and thoracic surgeon: Multispecialty group seeks second surgeon for balanced practice of adult cardiac, thoracic, and peripheral vascular surgery. Recent graduate preferred. Located on Florida's Gulf Coast, Tampa Bay area.

Please send response to H. Charles Campbell, MD, Diagnostic Clinic, 1551 West Bay Dr, Largo, FL 34640. 778J/L

Cardiothoracic surgeon, BE/BC, to join busy 1-man private practice in mid-Michigan. Excellent opportunity. Salary leading to partnership. Please send CV and references.

Please respond to Box 779. 779J/C

Cardiothoracic surgeon: BC/BE adult cardiothoracic surgeon wanted to join busy, established practice of four physicians. Physician will join large multispecialty group in metropolitan community of 130,000 in the upper Midwest. Affiliation with medical school and surgery residency available.

Please respond to Kathleen Toft, Director, Physician Recruitment, 737 Broadway, Fargo, ND 58123; or call 1-800-437-4010. 780J/L

Assistant surgeon: Cardiac, thoracic, or general surgeon with cardiac experience to join well-established 4-man group in the Midwest. Ideal for physician who desires low stress practice. Generous salary and fringe benefits. Please send curriculum vitae.

Please respond to Box 781. 781J/L

Cardiothoracic surgeon: Wanted to join a busy, well-established practice located in the Midwest. Prefer recent graduate, must be board certified or eligible, medical school affiliation possible. Respond with curriculum vitae.

Please respond to Box 782. 782J/L

Cardiothoracic surgeon needed to join established 2-man group in practice of adult cardiac, pulmonary, and vascular surgery. Must be board certified or eligible and graduate from a US medical school.

Please respond to R. W. Ruess, MD, 1834 Broadway, Cape Girardeau, MO 63701. 788K/A

Noncardiac thoracic surgeon wanted to join a group in northern New England. The practice would involve thoracic and general surgery. Must be board eligible or certified. Best in rural living. Please send CV.

Please respond to Box 791. 791K/A

Cardiothoracic and vascular surgeon urgently needed to join established practice in Midwest. Applicant must be BE/BC. Salary leading to full partnership. Please send CV and details of experience.

Please respond to Box 792. 792K/A

Thoracic and vascular surgeon, BE/BC, to join active (noncardiac) thoracic and vascular practice in central New Jersey. Please respond with curriculum vitae and details of experience. Salary leading to full partnership.

Please respond to Box 795. 795K/C

Cardiovascular and thoracic surgeon: Excellent opportunity for a board certified/eligible university-trained surgeon to join a new, growing department in a metropolitan New York community. Academic/private practice setting with excellent compensation. Experience in electrophysiologic surgery, artificial devices, and transplantation helpful. Please respond with curriculum vitae.

Please respond to Box 799. 799L/E

University of Florida seeks cardiovascular surgeon to join major teaching unit in Jacksonville, Florida, at University Medical Center. Candidate should be board eligible/certified in thoracic surgery. We seek someone with strong research and teaching interests. Position is tenure-accruing with academic appointment at Assistant to Associate Professor level, depending upon qualifications. Applicant recruiting deadline, April 1, 1993.

Forward curriculum vitae and names/addresses of three references to Eric Ceithaml, MD, Chairman, Cardiovascular Search Committee, University Medical Center, 655 W 8th St, Jacksonville, FL 32209. Affirmative action/equal employment opportunity employer. 801L/A

Cardiothoracic and vascular surgeon, board certified, board eligible to join an expanding three-man practice in the Rocky Mountain region. Please send CV and references.

Please respond to Box 802. 802L/E

Thoracic and vascular surgeon, BE/BC, wanted as associate/partner in private practice with clinical academic appointment in Providence, RI.

Please respond with CV and references to Albert K. Weyman, MD, 100 Highland Ave, Suite 304, Providence, RI 02906. 803L/A

Cardiovascular and thoracic surgeon to join established three-man private practice in Great Lakes area. Current practice is very busy in one location and new program is about to open in second location. Recent graduate is preferred, and must be eligible or certified in thoracic surgery. Please respond with CV.

Please respond to Box 804. 804L

Thoracic surgeon, BC/BE, wanted to join two-man extremely busy practice (non-open heart, non-vascular). Prefer candidate who has recently completed training. Excellent salary and benefits, leading to full partnership. Ideal location 20 miles south of Boston. Respond with CV and names of references.

Please respond to Box 805. 805L/E

General thoracic surgeon. The Massachusetts General Hospital and Harvard Medical School seek a highly qualified clinician, teacher, and scientist in general thoracic surgery. Training and experience in airway surgery and esophageal surgery required. Appointment would be at the rank of Instructor or Assistant Professor of Surgery at Harvard Medical School, depending upon qualifications.

Please reply with curriculum vitae and bibliography to Hermes C. Grillo, MD, Chief of General Thoracic Surgery, Massachusetts General Hospital, Boston, MA 02114. Harvard Medical School and Massachusetts General Hospital are affirmative action /equal opportunity employers. Women and minority candidates are encouraged to apply. 806L/B

Cardiac, thoracic, and vascular surgeon wanted to join a growing solo practice in western Pennsylvania. Practice excludes complex pediatric surgery and transplantation surgery. Immediate position available. ABTS certified or eligible. *Must* be willing to *work* in order to establish a continued growth.

Please send curriculum vitae and inquiries to Gene W. Manzetti, MD, 850 Clairton Blvd, Suite 2300, 51 Professional Plaza, Pittsburgh, PA 15236. 808L

The Division of Thoracic and Cardiovascular Surgery at the University of New Mexico School of Medicine in Albuquerque is seeking applications for a full-time faculty position at the Assistant/Associate Professor level for July 1993. We are looking for an individual with excellent skills in adult cardiac surgery and with specialized training in cardiac transplantation. The candidate must be board eligible or certified and have strong interest in research and teaching. This is an excellent opportunity for an individual interested in academic achievements as well as a good clinical experience.

Please forward curriculum vitae and three letters of recommendation to Jorge A. Wernly, MD, Chief, Division of Thoracic and Cardiovascular Surgery, University of New Mexico Medical Center-ACC2, Albuquerque, NM 87131. An affirmative action/equal opportunity employer. 809L/C

Cardiothoracic surgeon, board certified with 2 to 5 years experience. Wanted for practice in northeastern United States. Practice currently doing 500+ procedures and anticipates growth of 20%. Preferring surgeon with cardiac, thoracic, and vascular. Salary for 2 years, followed by full partnership. Please respond with CV.

Please respond to Box 810. 810L/A

Cardiothoracic/vascular surgeon: board certified in general surgery and BE/BC in thoracic surgery to join strong cardiovascular practice in western Pennsylvania. Major need for thoracic and vascular surgeon; cardiac surgery if desired. Excellent benefits. Detailed CV must accompany response. All replies treated confidentially.

Please respond to Box 811. 811L/E

Cardiothoracic surgeon, BE/BC, for Palm Beach County, Florida, busy, quality two-physician CVT practice.

CV to Kenneth M. Begelman, MD, 1599 NW 9th Ave, Boca Raton, FL 33486; FAX (407) 278-6887. 812L/A

SITUATIONS WANTED

General thoracic surgeon (BC), mature, looking for community with need, preferably Northeast or Southwest and group practice. Recent 10 years general surgical experience (BC) including laparoscopy.

Please respond to Box 741. 741H/A

Cardiothoracic surgeon, 35 years old, university trained, board certified with two years busy private practice experience. Seeks opportunity with new program, individual, or group in the Southeast.

Please respond to Box 757. 757J/C

Cardiovascular surgeon—34 y/o, ABTS, AOA, university trained—one year of clinical practice. Wishes to relocate to medium size community.

Please respond to Box 760. 760I/L

General thoracic and general surgery combined. Board certified. Recent graduate looking for an exciting practice. Interest in endoscopic and laser surgery.

Please respond to Box 790. 790K/D

56-y.o. Thoracic and cardiovascular surgeon, American graduate, university trained, numerous publications, advanced surgical degree. Recent 3 + 6 months tutorial in vascular and general surgery. Wishes to relocate.

Please respond to Box 794. 794K/A

Cardiovascular and thoracic surgeon, ABS certified, ABTS eligible, currently at a major university center. Excellent training in all aspects of adult cardiovascular and thoracic surgery including heart and lung transplantation. Extensive prior experience in the specialty in England. Seeks opportunity with private or academic group practice. Available July 1993. CV and references upon request.

Please respond to Box 796. 796K/A

Cardiothoracic surgeon, ABS, ABTS eligible, desires position with busy cardiothoracic group. Can assist or operate, considerable thoracic and ICU experience.

(504) 868-9358. 800L/A

FELLOWSHIPS

Surgical residents/fellows—Clinical residency/fellowship positions available in adult and pediatric cardiothoracic surgery. Large volume of cases. New Jersey license required. Excellent salary and benefits.

Please contact Lynn B. McGrath, MD, Chairman, Department of Surgery, Deborah Heart and Lung Center, 200 Trenton Rd, Browns Mills, NJ 08015; (609) 893-6611, Ext 359. 653L

Fellowship in adult cardiac surgery beginning July 1993 and available for one or two years in private program performing over 600 open heart procedures yearly. Cardiac surgery training required. ECFMG and visa qualified foreign applicants accepted.

Send curriculum vitae to Donald R. Kahn, MD, 817 Princeton Ave, Suite 300, Birmingham, AL 35211. 786K/A

Postresidency clinical fellowship available in cardiopulmonary surgery with group performing over 1,200 cardiac procedures per year. Up to 25% research opportunity option available. Complete training in cardiopulmonary surgery required. US graduates must be eligible for Oregon license. FMGs must be eligible for J-1 or H-1 visa. Fellowship for one to two years beginning January 1993 or July 1993.

Please send CV and three letters of reference to Albert Starr, MD, 9155 SW Barnes Rd, Suite 240, Portland, OR 19225. 789K/L

Cardiac surgical fellowship available at University of Massachusetts/St. Vincent Hospital Affiliate. Abundant adult cardiac experience, ideal interim position between residencies or awaiting job opportunity. Competitive salary, generous benefits. Mass licensure desirable. UMass is an equal opportunity employer.

CV and inquiries to John M. Moran, MD, St. Vincent Hospital, 25 Winthrop St, Worcester, MA 01604. 807L

THORACOSCOPY FOR THORACIC SURGEONS

Pericardiectomy, Blebectomy, Sympathectomy, Pulmonary Resection

These two-day advanced courses consist of four hours of didactics and 11 hours of hands-on laboratory. The techniques of thoracoscopic vagotomy, wedge resection, node dissection and other advanced procedures will be taught in detail. In addition, special emphasis will be placed on developing skills in thoracoscopic suturing and stapling techniques.

COURSE DIRECTOR
Karl A. Zucker, M.D.

COURSE MODERATOR
Mark J. Krasna, M.D.

FACULTY INCLUDES

Richard Heitmiller, M.D.
Rodney Landreneau, M.D.
Joseph Locicero, M.D.

The faculty is skilled in the use of hand instrumentation for the advanced thoracoscopic procedures. The operating stations are directed by thoracic surgeons who bring a wealth of clinical experience to the "hands-on" classroom.

Medcom Management International, Inc.
(410) 321-5481

LOCATION
United States Endoscopy Laser Institute
Baltimore, Maryland

Courses are limited to 18 participants.

UAB Division of Cardiothoracic Surgery

Thoracic Surgeon

University of Alabama at Birmingham

The Division of Cardiothoracic Surgery at the University of Alabama at Birmingham (UAB) seeks candidates for the Head of the Section of Non-Cardiac Thoracic Surgery.

UAB Division of Cardiothoracic Surgery has a very active clinical general thoracic surgical program and a growing lung transplant program. The successful candidate must be Board Certified in Thoracic Surgery with excellent clinical skills and strong academic interests. Position is tenure-accruing with appointment at an appropriate academic level. UAB offers an excellent compensation and benefits package.

Please respond with curriculum vitae and references to:

A. D. Pacifico, M.D.
Professor and Director
Division of Cardiothoracic Surgery
University of Alabama at Birmingham
Birmingham, AL 35294-0016

UAB IS AN EQUAL OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER
WOMEN AND MINORITIES ARE ENCOURAGED TO APPLY

INDEX TO ADVERTISERS

Baxter	A-19
BFW	A-25
CarboMedics	A-21
Datascope	A-12, A-13
DLP	A-7
Intermountain Health Care	A-28
Johnson & Johnson	A-29, A-30
Lankenau Hospital Medical Research Center	A-28
Medcom Management International	A-42
Medtronic	A-4, A-5, A-16, A-17, A-23
Miles	A-15
Promedica International	A-26, A-27, A-38
PSICOR	A-2
Sorin	Cover 2, A-1, Cover 4
St. Jude Medical	A-9, A-11
University of Alabama at Birmingham	A-42
W. H. Bookwalter	A-36
Classified Advertisements	A-39 through A-41

Address advertising inquiries to Art Carlucci, Elsevier Science Publishing, Inc, 655 Avenue of the Americas, New York, NY 10010; telephone: (212) 633-3806 (facsimile: (212) 633-3820).

BIOMEDICAL INFORMATION NOW AVAILABLE ON CD-ROM

TAKE A LOOK FOR YOURSELF

EXCERPTA MEDICA CD SERIES

- Anesthesiology
- Cardiology
- Drugs & Pharmacology
- Gastroenterology
- Immunology & AIDS
- Neurosciences
- Obstetrics & Gynecology
- Pathology
- Psychiatry
- Radiology & Nuclear Medicine

Full Text: Meyler's Side Effects of Drugs/Sedbase

FOR MORE INFORMATION PLEASE CONTACT ONE OF THE FOLLOWING EXCERPTA MEDICA OFFICES:

(Europe) Tel: +31-20- 5803230, fax: +31-20-5803222
(U.S.A.) Tel: 800-HLP-EMED; 212-6333971, fax: 212-6333913
(Japan) Tel: 03-59911337, fax: 03-35940539,

or send your request to:

Excerpta Medica, P.O. Box 548, 1000 AM Amsterdam, The Netherlands.

EM93

FROM BICARBON ON

BICARBON and
Copernicus's sp
both can claim t
represent a break
with the past.
BICARBON sets
a new standard
for heart valves
in terms of
performance
and reliability:
a new
"system of value
that everyone w
have to reckon
from now on.

NOT AVAILABLE IN THE U.S.A.

ETHICA

SORIN BIOMEDICA

RESEARCH AND TECHNOLOGY FOR HEALTH